MEDICAL ASPECTS OF ROAD SAFETY *

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THE first two deaths registered in Great Britain as due to motorcars were in 1896, while the first fatal accidents caused by motor-cycles were in 1902 (Martin 1957). From these small beginnings a terrible stream of deaths has followed. About 125,000 people have lost their lives in this country alone.

In 1958, 5970 persons were killed—1264 of them under the age of 20 and 1013 between 20 and 30. In the same year, 69,166 were seriously injured. This catastrophic loss and injury, particularly of the young, would undoubtedly have appealed to Gavin Milroy as a public-health problem demanding urgent attention. The problem is unique. All other epidemics throughout history have been due to the onslaught of external agencies, mainly the bacteria and viruses; but road accidents are caused by man himself. The community's responsibility should be recognised and vested in one authority, particularly as much existing knowledge awaits application.

Road, Vehicle, and Road User

The work of the Road Research Laboratory has resulted in many improvements in the design, construction, and lighting of roads.

Vehicle

On vehicle design and construction McFarland (1956, 1957) recommended among other things the removal of dangerous projections, the fitting of recessed-hub steering-wheels to reduce chest injury, the use of sponge-rubber padding to cover dashboards, and the use of seat-belts. But a higher standard of safety in the vehicle may mean a higher first cost, and manufacturers may not be able to reach this standard unless the public is willing to pay for it or forced to do so. Provins (1958) reviewed the effects of low and high environmental temperatures, and of air pollution by carbon monoxide, on tasks related to driving. Sustained temperatures below 50°F or above 87° appeared likely to impair driving efficiency, as did carboxyhæmoglobin levels above 12%. Methods of measuring and improving visibility from the driving seat were reported on by Fosberry (1958) of the Motor Industry Research Association. Studies of accident injuries in relation to the design and structure of the vehicles were undertaken at Cornell University (Moore 1957). This is the work on which recommendations for the use of seat-belts are based, for it showed that a frequent cause of fatal injury was ejection from the vehicle and that fatal and serious injuries were 80% fewer when seat-belts were used. Gissane (1959) designed a safety-cap for use by motorists. In Great Britain in 1958 the majority of the 1690 fatal accidents to vehicle drivers and passengers (Road Accidents 1958) were from head injuries, many of which would have been less serious if an efficient safety-cap had been worn.

The Road User

Many studies have been made of the road user. The Applied Psychology Research Unit, for example, has undertaken field studies of the actual task of driving. Psychologists, however, deal with the normal human organism and make no allowance for drivers with ocular defects or systemic disease—conditions which we have to consider here. At present, research in Great Britain covers only a small part of the work urgently required on human problems in road transport.

Of the various road users, the vehicle driver is not alone responsible for accidents; but it is he who holds the potentially lethal instrument. Driving is a *skill* which requires training, and, like other skills, it can be maintained at a high level only by regular practice. In London Transport the average time taken to train a driver who has never driven before is fifty hours at the wheel, spread over at least four weeks; experienced drivers may require almost as long to "unlearn" their faults. In some American States, drivers who have repeated accidents are sent to "driver clinics" for investigation and treatment. Such a procedure would be valuable if it could be clearly established that a particular driver had in fact experienced an excessive number of accidents compared with other drivers of the same age and sex who drive the same number of miles annually under similar conditions. These data are not generally available. The most baffling characteristic of road-accident statistics is the extreme difficulty of constructing an "exposed to risk" formula against which to consider them.

Epidemiology

The numbers of road casualties in 1926–58 are given in table I.

TABLE I—CASUALTIES FROM ROAD ACCIDENTS, GREAT BRITAIN, 1926–58

Year	Average Annual Numbers		
	Killed	Injured	Total
1926–29 (annual average)	5762	154,554	160,316
1930–34 (annual average)	7041	206,879	213,920
1935–38 (annual average)	6586	225,663	232,249
1939–45 (annual average)	Recording incomplete		
1946–49 (annual average)	4807	159,948	164,755
1950	5012	196,313	201,325
1951	5250	211,243	216,493
1952	4706	203,306	208,012
1953	5090	221,680	226,770
1954	5010	233,271	238,281
1955	5526	262,396	267,922
1956	5367	262,593	267,960
1957	5550	268,308	273,858
1958	5970	293,797	299,767

The annual number of deaths reached a peak in the early 1930s; the highest recorded was 7343 in 1934. In the past twenty-five years there has been some improvement, but this should be regarded less as a reason for complacency than as evidence that reduction in the death-rate is possible. (In 1952, for example, the deaths of pedestrians fell by over 10%: this was the year in which zebra crossings were introduced.) Since 1950 deaths have increased again, by about 20%. The increase in numbers injured may have been partly due to more complete recording of minor injuries. Some fluctuation was associated with motor-fuel rationing, which was in force, for example, from Dec. 17, 1956, to May 14, 1957.

* Abridged from the first Milroy lecture for 1960, delivered before the Royal College of Physicians of London on Feb. 2. The second lecture, with the references, will appear in a forthcoming issue.

The numbers of deaths from road accidents and from certain other conditions in 1957 are shown in table II.

In 1957, for the first time, deaths in road accidents exceeded those from all forms of tuberculosis. Deaths from diphtheria, whooping-cough, and acute poliomyelitis together were only a fifteenth of those caused by traffic accidents. The crude death-rate from road accidents at all ages is about equal to that from diphtheria in London in 1880–90 (Newsholme 1935). In males road accidents caused more deaths than tuberculosis, diabetes mellitus, chronic rheumatic heart-disease, peptic ulcer, or nephritis. Accidents in the home are about equally numerous, causing some 8000 deaths a year.

Road accidents are now the commonest cause of death in male adolescents and young adults. As fig. 1 shows, about a third of all male deaths in the years of promise, 20–24, are caused by road accidents. Morris (1955) estimated the chances that a man of 35 will sustain severe injury in a traffic accident before reaching the age of 65 as about 3%—and these are the safest years.

The road deaths in Great Britain in 1957 according to age and class of road user are shown in fig. 2. These figures are gross totals and take no account of the exposure-to-risk. The groups on which education, including propaganda, is focused are the young (male) motorcyclist, the child cyclist, and the elderly pedestrian.

TABLE II—DEATHS FROM CONDITIONS SPECIFIED, GREAT BRITAIN, 1957

International List no.	Condition	Deaths		
		Males	Females	Total
E810–E835 E840–E845	Road vehicle accidents	4186	1364	5550
001–019	Tuberculosis (all forms)	3898	1609	5507
055	Diphtheria	2	4	6
056	Whooping-cough	43	66	109
080	Acute poliomyelitis	150	87	237
260	Diabetes mellitus	1158	2484	3642
410–416	Chronic rheumatic heart-disease	3292	5812	9104
540, 541	Peptic ulcer	3993	1600	5593
550–553	Appendicitis	564	338	902
590–594	Nephritis and nephrosis	2597	2273	4870
660, 670–678	Maternal mortality	..	109	109

The mortality in road accidents per million living, by age and sex (fig. 3) emphasises the high rate in young adult males and in people over 70. There were 1057 road fatalities over the age of 70 in 1958, 904 (85%) of which affected pedestrians. The high death-rate in elderly male pedestrians is striking. Octogenarians were at least 20 years old in 1900; they grew up in the horse-and-buggy days and perhaps do not appreciate the high speed which oncoming modern vehicles may attain, nor the effect of their own reduced agility. Drivers, particularly young drivers, should be taught these mortality findings so as to give them a sense of care for elderly and perhaps infirm pedestrians. 40% of all fatal road accidents are to pedestrians.

A new era in prevention began with the studies of the late Sir Hugh Cairns on head injuries. He showed that most deaths of motor-cyclists were from head injury and advocated safety-helmets; but, even now, only about half the young men and women motor-cyclists wear them. In 1953–54 head injuries still accounted for 80% of fatal accidents to motor-cyclists (Grime 1958).

Table III shows that motor-cyclists are second to pedestrians in numbers killed. The large number of pedestrians killed shows the advantage to be gained if access were controlled, as on the railways. The relatively high rate of fatal accidents to motor-cyclists is shown in table IV. Clearly, parents and young men—and their pillion companions—should be warned of the dangers of motor-cycling without adequate head protection.

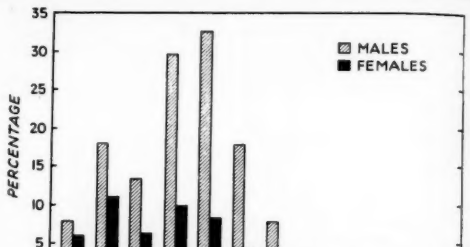

Fig. 1—Percentages of total deaths due to road accidents. Great Britain, 1957.

But the statistical picture is not all black. Since 1930, the number of fatal accidents has fallen steadily in relation to the number of vehicles licensed (fig. 4). The number per thousand vehicles registered decreases with increase in the number of vehicles using the roads. As the number of vehicles increases, people apparently become more skilled in avoiding accidents (Glanville 1954). Perhaps the increasing intensity of traffic prevents people from behaving as dangerously as they might. But it seems unlikely that we are yet motorising ourselves into a state of safety, and other reasons are probably responsible for this reduction in accident-rates.

In the United States road deaths fell from 39,628 in 1956 to 38,702 in 1957 and 37,000 in 1958—a reduction of 7% in three years. Over the same period fatal road accidents in Great Britain increased from 5367 to 5970. In the United States the death-rate per 10,000 vehicles registered in 1958 was 5·7, the lowest recorded (National Safety Council 1959); the corresponding figure in Britain was 8·0 (Road Accidents 1958). The lower figure in the United States may be associated with the lower proportion of vehicles to miles of road. Britain has the highest proportion of vehicles to miles of road of any country.

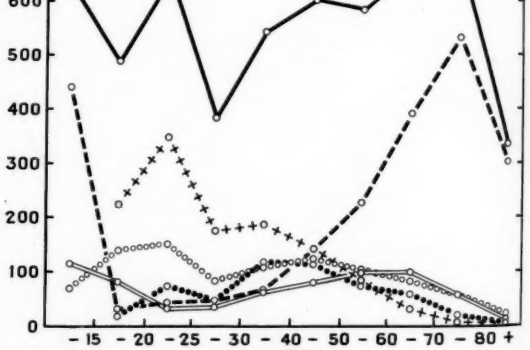

Fig. 2—Number of deaths in road accidents according to age and class of road user. Great Britain, 1957.

TABLE III—DEATHS IN ROAD ACCIDENTS, GREAT BRITAIN, 1957

Class of road user	No. of deaths
Pedestrians	2225
Motor-cyclists	1157
Moped-riders	47
Drivers of other vehicles	529
Pedal-cyclists	663
All passengers	929
Total	5550

In 1958 the death-rate in road accidents per 100 million vehicle-miles in the United States was 5·6, the lowest recorded; the corresponding figure in Britain was 10, also the lowest recorded.

The basing of fatalities on a denominator of total population figures is of limited value in the study of road-accident mortality trends. While the population has remained roughly constant, the number of motor vehicles registered has approximately doubled in the past ten years. It is therefore more realistic to use the number of miles actually travelled by road vehicles each year as the denominator for the calculation of mortality-rates. This mileage is obviously difficult to determine, but reasonably accurate estimates are given in Road Research (1958). The numbers of vehicle-miles travelled per annum are given for different types of road vehicle, but no estimates

TABLE IV—DEATHS PER MILLION VEHICLE-MILES, GREAT BRITAIN, 1956

—	No. of deaths	Millions of vehicle-miles travelled *	Deaths per million vehicle-miles
Motor-cyclists (including 176 passengers)	1250	4500	0·27
Occupants of other vehicles	1197	47,200	0·025

* Chandler and Tanner (1958).

can be made of the annual mileages travelled according to age and sex.

Fig. 5 gives the mortality in recent years according to vehicle-mileage travelled. Until 1954 there was a steady decline in the death-rate, expressed as mortality per million vehicle-miles, but since then there has been no improvement. This is probably one of the most useful statistics to indicate trends in mortality, but it takes no account of such factors as the ageing of the population. Studies of the death and accident rates in the several different ways described above are therefore required for a more complete picture of mortality trends.

Sex of Drivers and Accident-rates

Contrary to popular opinion, there is little evidence to show whether male or female drivers are the more liable to accidents.

Lauer (1952) analysed the reported accidents of men and women in Iowa. After allowing for women holding only a quarter of the licences, and after estimating that they drove only about a tenth of the total mileage, Lauer found no real

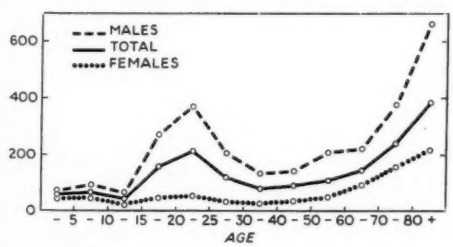

Fig. 3—Mortality in road accidents, by age and sex, per million living. Great Britain, 1957.

difference between the accident-rates of men and women drivers. A curious finding was that men improved their accident records after about five years' experience whereas women showed an improvement after the first year. This observation has not been confirmed by other workers.

Viteles and Gardner (1929) studied the accident experience of groups of men and women taxi-drivers and found that the women had fewer serious accidents than the men. The value of this study is limited, however, because the groups of men and women were not evenly matched for previous driving experience.

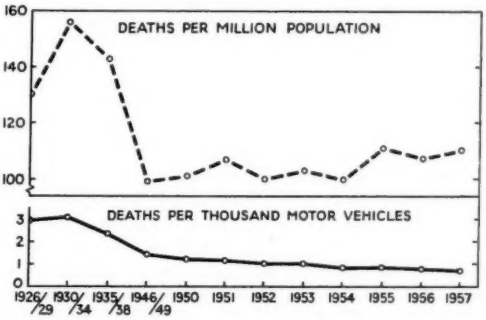

Fig. 4—Number of deaths in road accidents per million population and per thousand motor vehicles. Great Britain, 1926–57.

A study of Connecticut drivers (U.S. 75th Congress 1938) suggested that accidents per driver were fewer among women than men, but differences in exposure to accidents could not be fully taken into consideration.

Until strictly comparable groups of men and women drivers can be obtained, the existence of a sex difference in accident liability remains unknown. Studies of this factor might be of value, not merely to settle a difference of opinion between the sexes, but also as a lead to the further study of the reasons for any dissimilarity observed.

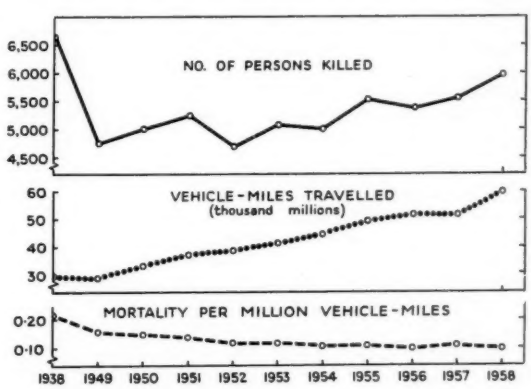

Fig 5—Mortality in all types of road accidents per million vehicle-miles travelled. Great Britain, 1938 and 1949–58.

Age of Drivers and Accident-rates

Below the age of about 65, younger drivers have more accidents than older ones. Thus McFarland et al. (1954), studying accident-rates of professional truck-drivers, found that the older men were less liable to accident. Again, Lauer (1952) found that among drivers of private cars those under 30 had the highest accident-rate.

The results of a study of the accident experience of London Transport drivers, by age, are given in table v.

TABLE V—LONDON TRANSPORT: CENTRAL BUS DRIVERS. AVERAGE NUMBER OF ACCIDENTS PER DRIVER PER ANNUM

Age attained in year of observation	Length of service as driver (years)				
	Under 4	4–8	9–13	14 and over	All service groups
Under 30 ..	2·409	1·770	..	..	2·386
30–39 ..	1·861	1·129	0·815	..	1·494
40–49 ..	1·576	0·943	0·832	0·677	1·077
50–59 ..	1·402	0·998	0·833	0·645	0·836
60–64 ..	1·316	0·869	0·934	0·623	0·728
Under 65 ..	1·876	1·022	0·843	0·640	1·173
65	..*	..*	..*	0·775	0·807
66	..	..	..	0·642	0·725
67	..	..	..	0·727	0·749
68	..	..	..	0·673	0·712
69	..	..	..	0·723	0·753
70	..	..	..	0·825	0·889
65 and over	..	..	..	0·721	0·766
All ages ..	1·876	1·002	0·843	0·650	1·159

* There are too few drivers over the age of 65 with less than 14 years' service to enable reliable rates to be calculated.

The average numbers of Central Bus drivers employed in 1957 and 1958 were 13,856 and 13,052 respectively, giving a total man-years of exposure for the two years of 26,908. All accidents, including minor ones involving no personal injury, were recorded, and totalled 31,198. Age is, of course, closely correlated with experience, and in order to study separately the effects of age alone, the drivers were divided into groups with different lengths of service. These men are all professional drivers who drive for about seven hours each working day of their lives. On average, a driver travels about 18,000 miles a year, and after fourteen years he will have driven about 250,000 miles, all in London traffic.

Table v shows that drivers under 30 have relatively high accident-rates, and for drivers with less than four years' service there is a steady improvement with increasing age. In the middle ages, the accident-rates of drivers with more than four years' experience show little variation with age. Experience has more effect than age. London Transport drivers may continue to the age of 70, subject to annual medical examination from 65 onwards. The number of drivers remaining in the service after 65 is relatively small. In fact, about half those who remain in the service until the age of 65 then retire voluntarily, so that those who continue after this age are a highly selected group. Nevertheless, the average accident-rate for these older drivers was 13% higher than the average rate for men under 65 with similar driving experience. Both rates are, however, notably lower than the rates for younger drivers with less than fourteen years' experience. The accident-rates for these older drivers appear to vary somewhat erratically with age, but these variations show some similarities with the retirement-rates of drivers and conductors. Retirement over 65 appears to take place as a process of continued selection—the fittest survive—so that an increase in retirements leads to a decrease in accidents.

Drivers of all ages with very short service have much higher accident-rates than drivers with long service. If this effect applies also to drivers of private cars, a practical application would be to continue training by means of occasional demonstrations and lectures during, say, the first two years after a licence is obtained. The inexperienced driver who drives only occasionally brings a double hazard on to the roads.

Much interest centres on the accident-rates of elderly drivers, but there are no reliable statistics of accident-rates of drivers over the age of 70. Insurance companies, before issuing a policy, sometimes require drivers over this age to submit a medical certificate of fitness to drive. They may have had unfavourable experience with these elderly drivers, and with some other classes of drivers, but their records do not provide satisfactory material for a study of accidents in relation to age. There are several reasons for this (Johnson and Garwood 1957): for instance, the insured car may be driven by different drivers at different times and accident experience is not therefore confined to the elderly owner-driver alone. Administrative action has, however, been taken in some countries. In New Zealand, from the age of 70 all drivers have to submit an annual certificate of medical fitness. The examinations thus necessitated sometimes place the family doctor or the consultant friend in difficulties, and it is suggested that they should be made by independent practitioners. In Portugal, medical examination is required before the issue of all licences, and these examinations are undertaken by a few specially appointed practitioners; this has also the advantage of maintaining a uniform standard. There is provision for an appeal against rejection.

Applied Psychology

The number of miles which the average driver travels before having an accident is impressive. When one considers the achievements of human beings on the roads in a detached way (for instance, by trying to think what sort of automatic device one could introduce to do the job instead) one is lost in admiration for their success. In 1958, the average driver would have had to travel about 200,000 miles before being involved in an accident resulting in injury to a person. At an average speed of 25 miles an hour, this represents a driving time of about eight thousand hours. As the average development time for an accident is probably about five seconds, or even less, drivers appear to possess remarkable powers of concentration. Perhaps the limit of human performance in this respect is being reached, but this unhappy view should not be accepted too readily.

The problem here is essentially one of vigilance. Mackworth (1950) found that vigilance was affected by environmental conditions and that people differed greatly in their abilities on the tests; but no reason could be discovered for these differences, which were unrelated to visual acuity or intelligence-test score. One practical application of vigilance studies lies in the teaching of anticipation, a very important quality for driving.

In spite of the emphasis placed on tests of reaction-time, the skill of driving—so far as it is related to accident prevention—does not depend solely on quickness of reaction. It seems obvious at first sight that drivers with the shortest reaction-times should be able to act most promptly in the accident situation and thus have fewer accidents than more slowly reacting drivers. That this idea may be misleading is shown by the fact that drivers aged 18–25, who have the shortest reaction-times, experience more accidents than middle-aged drivers. Young drivers give a better performance on psychokinetic tests generally. Allgaier (1938), for example, found that the tapping test was best performed in the 20s and that the best scores in a simulated driving task in a motor-trainer were given by drivers aged 15–25. It appears that as a man ages in the middle range, his reactions are slower, his hearing diminishes, his eye-hand coordination deteriorates—*but he becomes a safer driver*. This is probably because an essential part of the driving skill is the avoidance of accident situations, a factor which appears to be better developed in the middle-aged than in the young. Avoidance of the accident situation depends on the degree of care exercised, on experience, on the important quality of anticipation, and perhaps on other factors as yet unrecognised.

Laboratory and field studies of the nature of the driving task should provide information about the qualities required for safe driving. It is assumed—but the assumption may not be correct—that these qualities can be taught in their just proportions, and that the work of the psychological laboratory can be applied in the driving school. Laboratory studies are likely to be of use in improving the method of training more than its content, and perhaps in eliminating people who are defective in crucial qualities—if these can be identified (Broadbent 1960). The two main lines of investigation are (1) studies of the fundamental nature of human performance in relation to driving, and (2) the application of the results of applied psychological research to the training of drivers and other road users. There is need for an analytical study of the qualities required in driving, most of which can at present be approximately named and described but cannot yet be quantified.

Many studies have been made of accident-proneness. But the working environment of each driver is different; his exposure to risk of accident depends on such factors as the type of vehicle, the distance driven, and whether driving is mainly by day or night, in town or country. Even under the apparently constant conditions of London bus-routes, accident-rates are three times as high on some routes as on others.

There is, however, little satisfactory evidence to show that an individual driver's liability to accidents remains constant; nor has it been shown that a group of highly accident-prone drivers can be clearly separated from the rest. As Moore (1956) states, the most that can be said is that if all drivers had similar tasks there would be a group of accident-prone drivers, the size of which could be fixed by some arbitrary dividing line separating the prone from the not-prone. To prohibit people from driving on the ground that they belong to such a group would almost certainly be unjust in some instances. A study of 1000 public-service drivers in Finland was undertaken by Häkkinen (1958), who obtained a correlation of over 0·6 between the number of accidents experienced in one four-year period and the number of accidents experienced by the same drivers in the ensuing four years. This certainly shows that some drivers are likely to have accidents consistently, but Häkkinen was unable to find a reliable method of identifying accident-repeaters by laboratory experiment. It is important to distinguish between knowing that such people exist and being able to identify them.

In any one year in Great Britain, about 4% of the drivers have all the personal-injury accidents, but these drivers are not necessarily accident-prone. To study their proneness we should need to know whether they were involved in accidents in the following year, and this information is not available. Hence there is a tendency to replace the term "accident-prone" by "accident-repeater".

A recent study in this country is that of Davis and Coiley (1959), who defined accident-prone drivers as those who had sustained three or more accidents reported to the police between 1946 and 1958. Though their results did not confirm McFarland and Moseley's (1954) observation that accident-repeaters show personal qualities not found in safe drivers, Davis and Coiley draw attention to deficiencies in their own method of sampling and discuss plans for further research. It is surprising that this is the only investigation undertaken in the past twenty years in this country on drivers who have repeated accidents.

Further research is urgently needed to determine whether there is a group of constantly accident-prone persons among road users. If such a group could be identified, remedial measures might well include additional training. The community would have to decide whether to withdraw licences from substantially accident-prone drivers, temporarily or permanently.

Skilled activities, such as driving, tend to become disorganised under emotional stress. Emotional states also influence what is perceived in a situation, and inadequate or inappropriate reactions may be made by emotionally disturbed drivers, leading to a condition of temporary accident-proneness. Instances of accidents which occurred when drivers had been emotionally disturbed are well known, but nothing is known of the importance of such factors in the total of road accidents.

Psychological tests of many kinds have been applied to drivers in an attempt to distinguish those more liable to accidents from those less liable. Some of these tests, such as those of eye-hand coordination, of simple motor speed, and of choice-reaction, are performed worse by groups of drivers who have repeatedly had accidents than by the relatively accident-free. There is, however, considerable individual variation and it is not yet possible to use the results of such tests with any degree of accuracy to predict the performance of any one individual as a driver. The search for stable psychological characteristics of drivers which are significant in causing accidents has in general proved disappointing, but the study of psychosocial and temperamental factors appears more promising than the traditional approach by way of sensory and psychomotor abilities. Thus McFarland and Moseley (1954) developed a method of objective study which has identified certain personality characteristics among a group of drivers who had repeated accidents. These characteristics include egocentricity, aggressiveness, antisocial trends, and social irresponsibility; and their study led McFarland to formulate his view that "a man drives as he lives". This "style-of-life" approach provides a useful working basis for the selection of professional drivers; but its validity depends on the assessment of personality, which is notoriously difficult to measure. A curious anomaly is that some people who are quite reasonable in ordinary life become unreasonable when driving a motor vehicle.

It is possible that fatigue is a common cause of accidents. In Great Britain in 1958, among the 165,832 incidents reported to the police in which a personal contributory factor could be identified, there were only 409 in which fatigue (or "asleep") in a driver or cyclist was given as a contributory factor; but the police reports are likely to be incomplete in respect of fatigue. On the Pennsylvania Turnpike in 1952 and 1953, a driver was asleep in 13·2% of all accidents (Glanville and Moore 1955). In an unchanging environment vigilance decreases, and a lack of variation in perceptual stimulation may induce drowsiness. One practical application of this lies in the design of trunk roads, which should perhaps include factors to preserve the driver's alertness. There is no generally accepted definition of fatigue, but useful advice may be given to drivers about the need for adequate rest periods before driving, and about the advisability of resting for a few minutes every two hours or so on a long drive.

The concept of skill-fatigue, developed by Bartlett (1943), may be of importance in road accidents. A dis-

tinction is necessary between the type of fatigue produced by continued physical effort and that produced by a task requiring little muscular exertion but persistent concentration and a high degree of skill. The latter type of fatigue tends to occur during the first hours of work. A typical example is that of the driver at night who " halts at an intersection where there is no traffic light and waits patiently for the green; then, ' pulling himself together ', he dashes on, intent on the clear roadway ahead, and deriving no meaning from the headlights he sees approaching from the side " (*Lancet* 1957). Further studies will no doubt be undertaken on the nature of skill-fatigue. At present the only practical application might be to inform learner-drivers of the existence of this condition. It may be that some accidents at present attributed to such vague and rather meaningless factors as absentmindedness, lack of concentration, and inattention are in reality due to skill-fatigue.

Davis (1958) thought that explanations of accidents in terms such as lack of concentration and absentmindedness are unsatisfactory because either they do no more than give a name to what has obviously happened, or they suggest a cause without giving any insight into the way in which it might have operated to produce the particular accident.

Drugs and Driving

A reasonably efficient degree of human performance in many respects is necessary for the safe driving of a motor vehicle, and human performance may be adversely affected by many drugs which are in common use today, some of them obtainable without prescription. How far the use of drugs contributes to road accidents is unknown. Accidents in which a road user was noticeably under the influence of a drug are certainly rare, but the desirable clinical effect of mild sedation or the attempt to induce peace-of-mind by chemical means may affect driving safety. No laboratory studies on drugs, comparable with those on alcohol and driving, have so far been undertaken. Medical practitioners who prescribe drugs which may affect driving safety presumably have a duty to inform patients of the possible dangers of driving after taking the drug. Many patients are drivers, and there is here an added responsibility which must lie with the prescriber; unless he is told, the patient cannot be expected to know the possible effects and side-effects of the drug he is taking. For example, a bus driver was recently prescribed chloroquine sulphate, 800 mg. daily, at hospital. The side-effects of chloroquine include deposits in the cornea, paralysis of accommodation, and occasionally vertigo. This driver was advised at hospital to resume his normal work, no reference being made to his occupation.

Truly, as Donald Hunter has said, we are passing from the age of dangerous surgery and entering the age of dangerous medicine (Rose 1958). When I was a student it was sometimes cynically said that the only diseases we could cure were impetigo and scabies and not always those. Now there are powerful drugs to lower the blood-pressure, to alter the personality, to change the blood-chemistry, and some of these drugs may induce conditions which can adversely affect the patient as a vehicle driver. Hypnotics, sedatives, and tranquillisers should be prescribed with caution for drivers. The side-effects of anti-histamines vary considerably, and patients on these drugs should not drive until they have established by trial that they do not experience significant side-effects. Patients on ganglion-blocking agents should generally be advised not to drive, but other hypotensive drugs are probably safe where postural hypotension is not produced. The group of central-nervous-system stimulants, of which amphetamine is probably the most often prescribed, temporarily increase alertness and efficiency; but large doses may induce headache, agitation, irritability, and impaired concentration—in short, a condition of unfitness to drive. Fatigue and depression normally follow the initial stimulation. Miller (1957), who suggests that long-distance lorry drivers may be particularly exposed to this hazard, recommends that if the dosage of amphetamine does not exceed 10 mg., a driver may be permitted to prolong driving for a period not exceeding two hours; the drug should not be repeated on the same day. But in the interests of safety, drivers should probably be discouraged from taking any such drugs at all.

Patients under treatment with certain drugs, such as barbiturates, should be warned of the additive effects of alcohol. Many people, and probably many drivers, are now taking barbiturates or tranquillisers, and they should be made fully aware that the combined effects of alcohol and the drug may seriously impair their driving safety, even with an amount of alcohol which they would normally regard as " safe ".

Alcohol and Driving

In 1938 a committee of the House of Lords (H.L.52 Committee) said that " propaganda should be employed to train and fortify public opinion in the condemnation of persons who drink before driving—above all, to discourage the practice of ' one for the road ' ". A report on present knowledge of the relation of alcohol to road accidents has been published by the British Medical Association (1960).

Drew et al. (1959) studied the effect of measured blood-alcohol levels on the performance of 40 subjects in an experimental task resembling that of driving a vehicle on the road. With the low blood-alcohol levels reached there were no clinical signs of intoxication apparent to trained observers. Nevertheless, three-quarters of the subjects tested showed a measurable impairment of performance; this is the important finding. The chief problem is not the driver who is so intoxicated that he is physically unable to drive. The danger is with subclinical intoxication, in which a driver appears normal under clinical examination but his driving safety and efficiency are impaired.

The conclusion is inescapable that the consumption of alcohol by road users is responsible for a considerable proportion of road accidents. This is one of the most important problems in the promotion of road safety today.

" . . . Most people came into the service. The position of health in this respect has differed strikingly from that of education. The middle classes have found it more acceptable to go to a Health Service doctor or dentist than to send their children to state schools. This has been as much an advantage to the development of the service as it has been a disadvantage to the development of public education. It will be a great misfortune if access to private practice is made so easy as to restore the position where there is one standard of treatment for the better off and another for the rest.".—*New Statesman*, April 30, 1960, p. 632.

ANTICOAGULANT THERAPY IN ACUTE CEREBROVASCULAR ACCIDENTS

A CONTROLLED TRIAL

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AT present no specific form of medical treatment is of proven benefit for patients with a "stroke". Vasodilator drugs, corticosteroid therapy, and stellate-ganglion block have all been tried, but none has been proved of value when subjected to controlled clinical trial. This does not mean that medical treatment has no influence upon the acute illness. The appropriate application of supportive measures substantially affects mortality and the degree of functional recovery in survivors; these measures include physiotherapy for paralysed limbs, and the maintenance of fluid and electrolyte balance, nutrition, and pulmonary ventilation. But as yet neither the intracranial lesion nor its immediate effects upon nervous structures can be favourably modified.

Although the precise pathogenesis of many acute cerebrovascular lesions is uncertain, thrombosis is undoubtedly one of the mechanisms involved; and by analogy with their apparent usefulness in occlusive vascular disease in other sites, it seemed reasonable to postulate that anticoagulant drugs might be of benefit in cerebrovascular disease.

Hedenius (1941) first described their use in this context; but, although his impressions were favourable, his results were inconclusive. As with coronary-artery disease, therapeutic evaluation of these drugs in cerebrovascular disease has been slow and difficult; and some of the reasons have already been discussed in relation to long-term treatment (Hill, Marshall, and Shaw 1960).

In the acute stroke the principal difficulty lies in making a correct pathological diagnosis, for the same clinical picture may result from interruption of the same neural pathways by many different processes. Some are hæmorrhagic, as opposed to ischæmic, and obviously unsuitable for anticoagulant treatment. This distinction can sometimes be made reasonably accurately on the basis of such features as bloodstained cerebrospinal fluid, but no invariably reliable distinguishing criteria are known. For this reason the clinically descriptive terms stroke and cerebrovascular accident are considered preferable to labels such as cerebral thrombosis, which imply an accuracy in pathological diagnosis which present knowledge seldom justifies.

The other main difficulty in using anticoagulants for acute cerebrovascular accidents has been the fear that anæmic cerebral infarcts may become hæmorrhagic. This is based on theoretical grounds (Symonds 1956, Brain 1957) and on animal experiments (Wood et al. 1958), but in trials of anticoagulant therapy in cerebral infarction, both embolic and non-embolic, Carter (1957, 1959) did not encounter this complication.

In Carter's embolic series (1957) the progress of twenty-six patients who had anticoagulants for 14 days after the acute incident was contrasted with that of thirty-four patients not so treated; the mortality was lower and the number of recoveries greater in the treated group. Wells (1959) observed a similarly encouraging result in acute embolic infarction.

In his study of fifty-six cases of non-embolic cerebral infarction treated with anticoagulants, Carter (1959) found that those whose stroke was of slow onset might be helped, but not those with hemiplegia of sudden onset. Rose (1950) found no benefit from anticoagulants in non-embolic cerebral infarction; twenty-four treated patients progressed no better than might have been expected without treatment, and two died of cerebral hæmorrhage during treatment.

Ushiro and Schaller (1957) gave anticoagulants to twenty-six patients with cerebrovascular accidents, but they did not distinguish between thrombotic and embolic cases; comparing the results with those in thirty-nine similar but untreated cases, they found no appreciable difference in the mortality-rate, the incidence of complications, or the natural course of recovery. Fisher (1958), however, reported more favourably on anticoagulants used in fifty-eight patients with cerebral thrombosis at various stages. He divided them into five groups, ranging from those who experienced transient ischæmic attacks only with no significant neurological deficit, to those with a fully developed stroke and maximum neurological deficit. Only the last group was not improved, and Fisher emphasised the value of anticoagulants in the progressively evolving stroke.

Millikan et al. (1958), from wide experience of anticoagulant therapy in various types of cerebrovascular disease, concluded that the four main indications for its use are: (1) intermittent insufficiency in the vertebrobasilar system, (2) intermittent insufficiency in the carotid system, (3) thrombosis in the vertebrobasilar system with infarction, and (4) actively advancing occlusion of the carotid system.

While these studies may suggest that anticoagulants are of value in particular situations they do not provide an adequate basis on which to decide for or against anticoagulant therapy in the majority of individual patients with a stroke. We therefore planned the present trial in an attempt to assess the value of anticoagulants in relation to the common therapeutic problem of the acute cerebrovascular accident of recent onset, when a hæmorrhagic causal lesion has been excluded as far as possible clinically, but regardless of the precise anatomical site of the occlusion. We decided to exclude cases of cerebral embolism resulting from conditions such as rheumatic heart-disease or myocardial infarction, because they differ in many respects from the more common non-embolic infarctions, and because others had suggested that their response to anticoagulant therapy is different. In cases of embolism there is often no intrinsic disease of the cerebral arteries, whereas such disease may influence the anastomotic circulation in non-embolic cases.

All patients in the trial were submitted to cerebral angiography, although we realised that this might be neither necessary nor practicable should anticoagulants prove generally beneficial in acute strokes. Our aim was to improve diagnostic accuracy and to assess the value of angiography in this respect (Bull, Marshall, and Shaw 1960).

In view of the difficulty of assessing therapeutic results in a condition of such variable and unpredictable pattern, we considered it essential to test anticoagulants in a strictly controlled trial. Its primary aim was to assess the influence of anticoagulant therapy on the immediate mortality—i.e., within 6 weeks of the cerebrovascular accident—but, in addition, any possible effects on late mortality or recurrence were sought by regular follow-up of patients after discharge from hospital.

The Trial

Method

Patients included in the trial were under 70 years of age. During the 72 hours before admission to hospital they had sustained severe and persistent disturbance of brain function thought to be due to an acute cerebrovascular lesion other than hæmorrhage, extradural or subdural hæmatoma, aneurysm, or arteriovenous malformation, and provided no source of embolism was apparent in the heart.

Because the majority of patients were sent by the Emergency Bed Service and were not referred as diagnostic neurological problems no unusual selection operated at this stage. The diagnosis was based on the history, clinical examination, lumbar puncture to confirm the absence of blood from the cerebrospinal fluid, plain radiographs of the skull, and angiography of the appropriate cerebral vessel. While appreciating that more extensive angiography might sometimes be more informative, we decided to limit the examination to a single vessel (carotid or vertebral) to maintain uniformity. Patients with severe hypertensive retinopathy, left ventricular failure, evidence of peptic ulceration, bleeding disease, or severe hepatic or renal disease, were excluded from the trial.

TABLE I—AGE AND SEX DISTRIBUTION OF PATIENTS

Age (years)	Treatment group			Control group		
	Males	Females	Total	Males	Females	Total
30–39	1	1	2	0	2	2
40–49	4	3	7	0	3	3
50–59	7	6	13	4	5	9
60–69	2	2	4	6	5	11
Total	14	12	26	10	15	25

Patients regarded as having a non-embolic infarction after the above investigations were included in the trial only if the investigations had been completed so that treatment could be started within 72 hours of the onset of the illness. They were randomised in pairs between two groups; no attempt was made to match them on the basis of age, sex, or any particular feature of their disease. One group had anticoagulant therapy, and the other acted as control.

The patients in the treatment group received an initial dose of phenindione (' Dindevan ') 300 mg. by mouth or by intragastric tube. 12 hours after angiography they were given three doses of heparin (12,500 units) intravenously at 6-hourly intervals. Earlier administration of heparin has occasionally caused excessive bleeding from the site of arterial puncture. From the 2nd day onwards, treatment was continued with phenindione twice daily by mouth, the dose being regulated by daily prothrombin estimations using the Quick one-stage test. The prothrombin-time was kept at two to three times the control time; treatment was continued for 21 days and then gradually withdrawn. Both treatment and control groups were given the same general care and physiotherapy. Uniformity in the management of both groups is important because factors such as bronchial obstruction and pulmonary infection, urinary infection, and fluid or electrolyte imbalance influence mortality.

Because of uncertainty regarding the efficacy and hazards of anticoagulant treatment, it was desirable to subject the results to continuous analysis so that the trial might be concluded immediately a definitive answer emerged. Classical tests of significance are generally inappropriate for this type of analysis, and the sequential method (Armitage 1954) was therefore adopted.

The Patients

Fifty-one patients were included in the trial, twenty-four men and twenty-seven women. Twenty-six patients were treated, and twenty-five served as controls. The distribution by age and sex to the two groups is shown in table I. Fourteen patients (27%) in the series were below the age of 50. Table II shows the anatomical site of the vascular lesions as judged clinically or angiographically. In thirteen instances, including all the cases of internal-carotid thrombosis, the occluded vessel was demonstrated angiographically.

TABLE II—SITE OF LESIONS

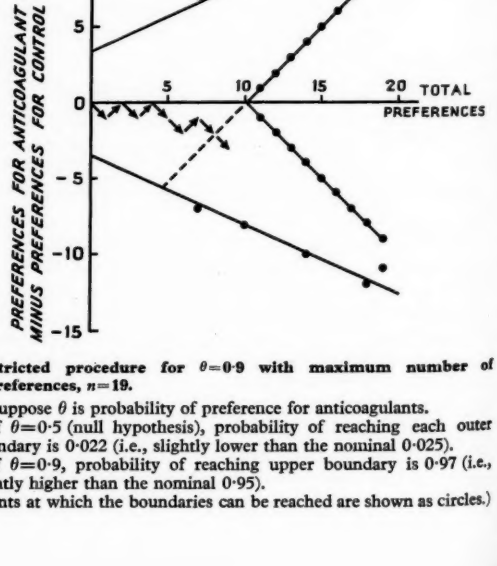
Site	Treatment group			Control group		
	Males	Females	Total	Males	Females	Total
Middle cerebral ..	10	9	19	4	10	14
Anterior cerebral ..	0	0	0	2	1	3
Internal carotid ..	2	2	4	2	2	4
Vertebrobasilar ..	2	1	3	2	2	4
Total	14	12	26	10	15	25

The incidence of hypertension on the basis of initial hospital blood-pressure readings is misleading because the intracerebral lesion itself may cause elevation or depression of the blood-pressure; an accurate premorbid reading is seldom available. But taking the mean of all hospital readings, including those in the recovery phase, ten patients had a mean diastolic pressure of 110 mm. Hg or above; of these four were in the treatment group and six were controls.

Results

The figure shows the sequential chart on which were plotted the results as they became available. Survival or failure to survive for 6 weeks from the start of treatment was the criterion on which results were based.

On admission to the trial patients were randomised in pairs, one to the treatment group and the other to the control group. The analysis took cognisance only of those pairs in which the two members behaved dissimilarly—i.e., one survived while the other died (untied pairs); no regard was taken of pairs in which both members survived or both died (tied pairs). When in an untied pair the treated member died, an arrow was plotted pointing downwards and to the right, whereas when a control member died the arrow pointed upwards and to the



Restricted procedure for $\theta=0{\cdot}9$ with maximum number of preferences, $n=19$.

Suppose θ is probability of preference for anticoagulants.

If $\theta=0{\cdot}5$ (null hypothesis), probability of reaching each outer boundary is 0·022 (i.e., slightly lower than the nominal 0·025).

If $\theta=0{\cdot}9$, probability of reaching upper boundary is 0·97 (i.e., slightly higher than the nominal 0·95).

(Points at which the boundaries can be reached are shown as circles.)

TABLE III—RESULTS OF TRIAL

Result	Treatment group	Control group
Early (within 6 weeks):		
Deaths	6	3
Further ischæmic episodes	0	2
Late (6 weeks to 6 months):		
Deaths	2	4
Further ischæmic episodes	3	0

right. The horizontal axis thus represents the total number of untied pairs. The vertical axis represents the number of untied pairs showing preference for anticoagulant treatment minus those showing preference for control treatment. Thus if the apex of the plot registers a plus value it indicates a trend in favour of anticoagulant treatment, whereas a minus value (as in the figure), favours the control.

The statistical design was a " restricted procedure " of the type tabulated by Armitage (1957), but further calculations made since 1957 allowed the maximum number of untied pairs to be reduced from twenty-two to nineteen, and the appropriate boundaries are shown in the figure. If the plot had reached the upper boundary, it would have indicated a difference in favour of anticoagulants, or if it had reached the lower boundary, it would have indicated a difference in favour of the control treatment. Achieving either of the end boundaries would mean that no significant difference exists between anticoagulant and control treatment.

TABLE IV—CAUSES OF DEATH

Treatment group				Control group			
Case no.	Sex	Age (yr.)	Diagnosis	Case no.	Sex	Age (yr.)	Diagnosis
74977*	M	57	Brain-stem infarction	74923	F	69	Brain-stem infarction
76755	F	37	Cerebral infarction	78689	M	58	Bilateral cerebellar hæmorrhagic infarction
79902	F	52	Bilateral cerebral hæmorrhages	83612	F	58	Multiple cerebral softenings
82435	M	39	Cerebral hæmorrhage				
84237	F	59	Multiple cerebral infarcts				
85678	M	55	Cerebral hæmorrhage				

* Postmortem not performed.

When the eighth untied pair had been observed, five favoured the control treatment and three the anticoagulant treatment. The plotted path had reached the dotted line shown in the figure, indicating that a verdict in favour of anticoagulants was no longer possible with the experimental design chosen. Clearly there was no justification for continuing the trial merely to detect a significant difference in favour of control treatment should such exist, and the trial was accordingly stopped with no significant differences demonstrated. A few more results of pairs already in the trial became available with the completion of 6-week follow-up periods after the dotted line had been reached. In all, twenty-six patients were treated with anticoagulants of whom twenty survived to 6 weeks: twenty-five patients were in the control group of whom twenty-two survived to 6 weeks.

The results, including late deaths during a 6-month follow-up period, and further cerebral ischæmic episodes during treatment and follow-up, are summarised in table III. No conclusions can be drawn from this table. Postmortem examinations (Prof. William Blackwood and Dr. W. G. P. Mair) were performed on eight of the nine patients who died within the first 6 weeks, and the causes of death are shown in table IV. In the treated cases the infarcts did not differ morphologically from those normally encountered in untreated patients, and hæmorrhagic infarction was not seen; three patients died of cerebral hæmorrhage, however. Study of the case-histories of the patients who died in respect of age, blood-pressure, severity of initial lesion, and time-interval before treatment was started, did not show that the unfavourable results were confined to any particular subgroup. All eight patients with internal-carotid occlusions in both groups survived, whereas four of the seven patients diagnosed as having vertebrobasilar occlusions died—two being in the treatment group and two in the control. But no conclusions can be drawn from such small numbers. No hæmorrhagic complications of therapy arose from sites other than the central nervous system.

Discussion

This trial was undertaken in an attempt to answer a specific practical problem regarding the management of one of the commonest medical emergencies. The knowledge that anticoagulants have been reported to benefit certain groups of patients is not always helpful in planning the immediate treatment of an individual patient. Cases can be classified more easily in retrospective analysis than on the day of admission to hospital, when one may have to decide promptly whether to give anticoagulants. The retrospective formulation of the illness takes account of its total course, sometimes including necropsy findings, and it never gives a satisfactorily quantitative balance between therapeutic successes and failures, misdiagnoses, and complications of treatment. Of the patients with strokes in whom benefit from anticoagulants may be expected on the basis of reported series, only a few—such as those with insufficiency and vertebrobasilar syndromes —are clinically distinguishable in the early stages. For example, without a period of observation during which the opportunity for effective treatment may be lost, one cannot tell that a stroke is still evolving; and the majority of cases of acute carotid occlusion present a clinical picture which is indistinguishable from that associated with middle-cerebral occlusion (Silverstein 1959). The physician is therefore faced with a difficult choice. Either he must treat with anticoagulants all patients who have had a stroke and in whom there are no obvious contraindications, in the hope that an unpredictable proportion of them will benefit; or alternatively he must withhold anticoagulants knowing that he may deny a possibly effective treatment to some of his patients.

Our trial was designed in relation to these considerations: the criteria of selection of the patients were not precise, but they seemed appropriate and generally applicable to the clinical problem. According to our criteria of selection and management, even with the added refinement of cerebral angiography in all cases, we were unable to show any benefit from anticoagulant treatment. More than this cannot be inferred from the data. Although the trend of the results may suggest that anticoagulants may even be hazardous when used as in the trial, this has not been proven. Had the trial been continued the lower boundary might have been reached, showing that treatment was definitely harmful; but alternatively it might have proceeded to a point where no significant difference emerged between treatment and control groups. There was obviously no justification for continuing the trial simply to make this distinction.

Analysis of the causes of death shows that preponderance in the treatment group is attributable to the three

cases of cerebral hæmorrhage. These were clearly massive intracerebral extravasations, and not simply hæmorrhagic infarctions. One hæmorrhagic infarction was encountered among the fatalities in the control group, but there was none in the treatment group as had been forecast. The most likely explanation of why these cases of hæmorrhage were in the treatment group is that the original stroke was in fact due to hæmorrhage which was mistakenly regarded as infarction despite lumbar puncture and cerebral angiography. Barron and Fergusson (1959) have drawn attention to the large number of fatal cerebral hæmorrhages among the extensive reports on anticoagulant therapy in cerebrovascular disease. Therefore so long as our ability to distinguish cerebral hæmorrhage from infarction remains poor, so long will the use of anticoagulants for cerebrovascular accidents carry the risk of aggravating a misdiagnosed cerebral hæmorrhage. The limitations of diagnosis in cases of stroke are further emphasised by two examples in this series: despite typical presentations and normal angiograms and cerebrospinal fluid, these patients had cerebral tumours. One was in the treatment group, the other in the control; both survived to 6 weeks and so did not influence the analysis.

This study in no way refutes the findings of previous workers who have reported benefit from anticoagulants in limited subgroups of cerebrovascular accidents. It suggests, however, that these subgroups may be difficult to recognise in the acute phase of the illness when treatment has to be initiated; and that, as a practical therapeutic measure for most patients with strokes, anticoagulants are not to be recommended. A controlled trial is, we think, the only satisfactory method of assessing the value of treatments of potential hazard. The sequential form of analysis is suited to such trials because it allows detection of differences at a relatively early stage.

Summary

A controlled trial of anticoagulant therapy was made in fifty-one patients with a diagnosis of acute non-embolic non-hæmorrhagic cerebrovascular accident. Patients were randomly allocated to treatment or control groups, and the results, measured by survival to 6 weeks, were analysed by a restricted sequential procedure. The conclusion was that anticoagulants, when used according to the criteria of selection and management of the trial, are not of value.

We are greatly indebted to Dr. P. Armitage for the detailed statistical design to suit the particular requirements of this trial; and to the Nuffield Foundation for financial support.

The results of this trial were communicated at a Conference on Occlusive Vascular Disease at the Royal College of Physicians in November, 1959, the proceedings of which are to be published by the Pitman Medical Publishing Co. Ltd.

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SERUM-TRIGLYCERIDE LEVELS IN SOUTH AFRICAN EUROPEANS AND BANTU AND IN ISCHÆMIC HEART-DISEASE

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STUDIES on the epidemiology of ischæmic heart-disease have shown a pronounced difference in the prevalence of the disease in population groups subsisting on diets of varying lipid composition. In general, population groups having a high fat caloric intake (as in Western countries) tend to have a higher prevalence of the disease than groups subsisting on a low fat caloric diet, such as the South African Bantu.

Most of these studies have been confined to an examination of the influence of dietary factors on serum-cholesterol levels, and relatively few reports have dealt with the manner in which fasting serum-triglyceride levels may be affected.

Interest in serum-triglyceride concentrations in health and disease has been greatly stimulated since it has been shown that hyperlipæmia may not only accelerate blood-clotting (Duncan and Waldron 1949, Fullerton et al. 1953, Poole 1955, O'Brien 1955, Buzina and Keys 1956, MacLagan and Billimoria 1956, MacDonald and Edgill 1957), but also increase blood-viscosity, as well as producing increased adhesiveness and aggregation of red blood-cells (Swank 1951, 1954, 1956, Cullen and Swank 1954). Close correlation has recently been shown between raised fasting-serum-triglyceride levels and the prevalence of ischæmic heart-disease by Albrink and Man (1959). Other workers (Hatch et al. 1955, Albrink and Man 1956, Ahrens 1957, Havel 1957a, 1957b, Ahrens et al. 1957, 1958, Dole et al. 1959, Kuo and Carson 1959) have shown that variations in both the fat and carbohydrate composition of the diet may rapidly produce distinct changes in serum-triglyceride concentration, with only slight immediate effects on serum cholesterol and phospholipid levels.

Accordingly we felt that valuable information might accrue from a study of fasting serum-triglyceride levels in the two main racial groups living in South Africa: (1) the European, whose diet in the main is similar to that of most people of the Western hemisphere (i.e., containing approximately 40% of calories derived mainly from animal fat), and among whom the prevalence of ischæmic heart-disease is high; and (2) the Bantu, whose diet in general contains less than 15% of calories from fat, is high in carbohydrate content, and among whom the prevalence of ischæmic heart-disease is very low.

We describe here the findings for these two population groups subsisting on their habitual diets.

Cases Studied

Those investigated were 46 healthy European males, aged 18–62 years; 23 healthy European females (18–46 years), all premenopausal; 23 European patients with ischæmic heart-disease, aged 33–67 years (2 males less than 40 years, 6 males and 3 females 41–50 years, 7 males and 2 females 51–60 years, and 3 males more than 60 years); and 57 healthy Bantu males aged 20–60 years.

The healthy European subjects were active members of the technical staff of the South African Institute for Medical Research, who showed no clinical evidence of ischæmic heart-disease. X-ray examination of the heart, chest, and lungs in each subject showed no abnormalities. Electrocardiography was not carried out. The patients with ischæmic heart-disease were at the Johannesburg General Hospital; all had been

admitted on account of recent acute myocardial infarction. This diagnosis was based in each case on clinical evidence and was confirmed by electrocardiography. Blood samples were in each case taken during the first week after infarction. These patients had received no anticoagulant therapy before this investigation was carried out. The Bantu subjects consisted of mineworkers who undergo careful physical examination before being accepted for employment, and were clinically normal.

In the case of the European subjects blood specimens were drawn before breakfast after an overnight fast of twelve to fourteen hours. This was not possible in the case of the Bantu volunteers. The Bantu mineworker has a light breakfast before starting an eight-hour shift underground without any food intake during the shift, except in some cases where a midday drink of " kaffir beer "—a non-alcoholic carbohydrate beverage —was taken. All specimens of blood were drawn immediately after the day's shift had been completed and before the subjects consumed any food.

Methods

Triglycerides were estimated by several methods, all of which gave close correlation. A modification of the method of Van Handel and Zilversmit (1957), using activated silicic acid and isopropyl ether, was used for the initial separation of serum-triglycerides, cholesteryl esters, and free cholesterol from phospholipids, and the extracts obtained in this manner were hydrolysed by the method of Carlson and Wadstrom (1959). Liberated glycerol was then estimated fluorimetrically by the method of Mendelsohn and Antonis (1960). The phospholipid-free extracts were also analysed for ester groups by the method of Stern and Shapiro (1953), and for cholesteryl esters by the method of Schoenheimer and Sperry, as modified by Sperry and Webb (1950). Triglyceride values were then calculated by subtraction of the cholesteryl-ester content from that of total ester groups. Total lipid extracts were fractionated by the silicic-acid chromatographic technique of Barron and Hanahan (1958), and triglycerides were estimated on the appropriate fractions by the above techniques, and also by hydrolysis and titration of the liberated fatty acids. Since serum phospholipid and total-fatty-acid levels were also estimated on the samples (by the methods of Fiske and Subbarow [1925] and Stern and Shapiro [1953], respectively), serum-triglycerides were calculated by the method of Thannhauser and Reinstein (1942). In general, correlation was good, except in the case of some of the older normals and the patients with ischæmic heart-disease, where lower triglyceride values were obtained by calculation than were found experimentally. Triglyceride polyenoic fatty acids were estimated after alkali isomerisation by the ultraviolet spectrophotometric method of Holman and Hayes (1958).

TABLE I—FASTING SERUM-TRIGLYCERIDE LEVELS (MG. PER 100 ML.)

Age (yr.)	Bantu males			European males			European females			Ischæmic heart-disease		
	No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean	S.D.	No.	Mean	S.D.
<30	26	80	±21	16	86	±26				M.		
31–40	16	73	±19	12	97	±28	18	69	±20	18	197	±62
41–50	9	66	±17	7	174	±84	5	65	±20	F.		
51–60	6	68	±12	8	174	±53				5	192	±53
>60	..	..	..	3	139	±49						
Whole group	57	75	±20				23	68	±20	23	196	±61

For Bantu males, the decrease in the mean serum-triglyceride level with age is not significant since the regression equation for age against serum-triglyceride level is not significantly different from zero (correlation coefficient 0·17).

For European males, both the means and the standard deviations of the under-40-year age-groups are significantly different from those of the 41-60-year age-groups.

The mean for the cases of ischæmic heart-disease is not significantly different from that of the 41-60-year European males.

Results

Serum-triglyceride Concentration

Individual fasting serum-triglyceride levels for the 152 subjects investigated are shown according to age in fig. 1.

The majority of the young subjects of both races and sexes have values of under 114 mg. per 100 ml., shown by the upper interrupted line. This value has been calculated from the results obtained for the Bantu subjects as the mean+1·96×S.D. Only 2·5% of these subjects will therefore be expected to have serum-triglyceride levels above this value. Comparison of the serum-triglyceride levels for the other groups shows that all the European premenopausal females have triglyceride levels lying below this value; in the case of the European males, 6% of the under-30, 25% of the 31–40, 86% of the 41–50, and 88% of the over-50 age-groups, as well as over 96% of the heart-disease cases, had serum-triglyceride concentrations greater than 114 mg. per 100 ml.

Serum-triglyceride levels of Bantu males and European females (premenopausal) show no age trend. Values for European males, however, show a distinct age trend with a widening scatter. Ischæmic-heart-disease patients at all ages have serum-triglyceride levels very much higher than those of young subjects, but only slightly higher than a large proportion of the older European males, and no age trend is apparent. These results have been examined statistically, and the mean value for each group of subjects divided by decade, is shown in table I.

For Bantu males the mean serum-triglyceride level decreases slightly from age 20 years through to age 50 years, but this fall is not significant since the regression on age gives a correlation coefficient (0·17) not significantly different from zero. Since the standard deviations for the various decades are also not significantly different, the Bantu group can be considered homogeneous with a mean serum-triglyceride level of 75±20 mg. per100 ml.

European females (premenopausal) under 46 years of age show no age trend, and have a mean serum-triglyceride

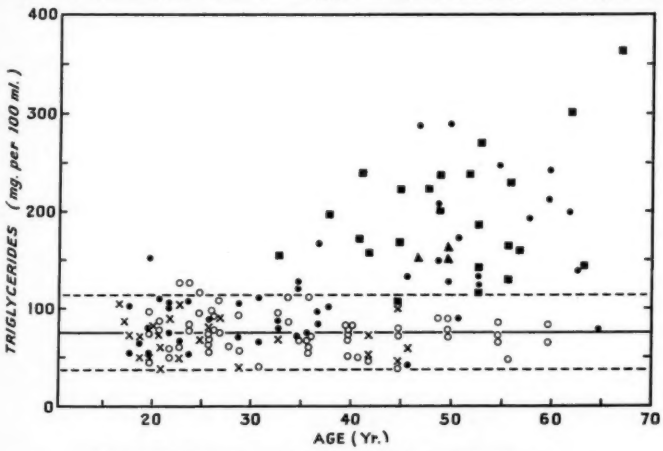

Fig. 1—Fasting serum-triglyceride levels at different ages.

The continuous line represents the mean (75 mg. per 100 ml.), and the interrupted lines upper and lower limits of normal (mean±1·96× S.D.) for the Bantu subjects at all ages (114 and 36 mg. per 100 ml., respectively). Open circle represents Bantu males; closed circle, European males; cross, European females; triangle, 3 postmenopausal European females; and square, patients with ischæmic heart-disease.

TABLE II—TRIGLYCERIDE POLYENOIC-FATTY-ACID COMPOSITION (MEAN ± S.D.)

Group	No.	Total fatty acids (mg. per 100 ml.)	Percentage of total fatty acids				
			Dienoic	Trienoic	Tetraenoic	Pentaenoic	Hexaenoic
European females <46 yr.	13	74±19	27·1±3·2	6·4±0·8	5·9±1·1	1·5±0·3	3·9±0·9
Bantu males all ages	57	71±19	30·7±2·1	6·9±1·5	8·3±2·8	2·7±0·7	5·8±1·5
European males 18–30 yr.	8	72±21	26·6±1·6	6·5±1·3	5·5±1·0	1·7±0·5	3·9±1·5
European males 31–40 yr.	8	86±18	21·7±4·5	5·6±1·1	5·5±1·5	1·9±0·6	4·2±1·6
European males 41–70 yr.	13	186±55	20·2±3·6	4·0±1·4	5·8±1·8	1·9±0·7	4·9±1·3
Patients with ischæmic heart-disease, all ages, both sexes	23	188±58	18·1±2·5	3·2±1·0	4·0±1·4	1·0±0·7	4·1±1·8

Bantu mean serum-triglyceride dienoic, tetraenoic, and hexaenoic fatty-acid percentages are significantly greater than those of European males under 30 years of age ($P<0.001$, $P<0.01$, and $P<0.01$, respectively).
European males under 30 years and European females under 46 years of age have polyenoic-fatty-acid patterns not significantly different from each other. Their mean serum-triglyceride dienoic-fatty-acid percentage is significantly greater than that of European males over 30 years of age and ischæmic-heart-disease cases ($0.01<P<0.02$).

level of 68±20 mg. per 100 ml. 3 European females over age 46 years, all postmenopausal, had higher levels—150 mg., 150 mg., and 158 mg., per 100 ml.

European males under 30 years of age have a mean serum-triglyceride level of 86±26 mg. per 100 ml., not significantly different from the values of the Bantu and European females. For the 31–40-year group the corresponding mean is 97±28 mg. per 100 ml. After this decade, however, there is a clear upward trend, and the means for the next two decades are 174±84 mg. and 174±53 mg. per 100 ml., respectively. Ischæmic-heart-disease patients whose ages ranged from 33 to over 60 years had higher serum-triglyceride levels than all the other subjects, but no age trend was apparent in the few cases investigated. The mean for this group was 196±61 mg. per 100 ml.

The standard deviations of the 31–40 and 41–50 year European male groups are significantly different at less than the 2% level (variance ratio=9·55; 2%=7·72). Fig. 2 shows the means and the 95% confidence interval of the means plotted decade by decade for the Bantu and European males. For the European males, both the means and the standard deviations increase significantly with age.

Means are significantly different where no overlapping occurs of the 95% confidence limits, as depicted by the interrupted lines. Standard " t " test or regression analysis is not relevant because of the significant difference in the standard deviations (Kendall 1951).

The figure also clearly shows that the Bantu mean is significantly different from those of the European male groups over the age of 30 years.

The mean value for the ischæmic-heart-disease cases was higher than those of the European males aged 41–50 and 51–60; but the differences were not statistically significant.

The frequency distribution of the serum-triglyceride concentration for the four groups—Bantu, European males under 40 years, European males over 40 years, and ischæmic-heart-disease cases—is compared in fig. 3.

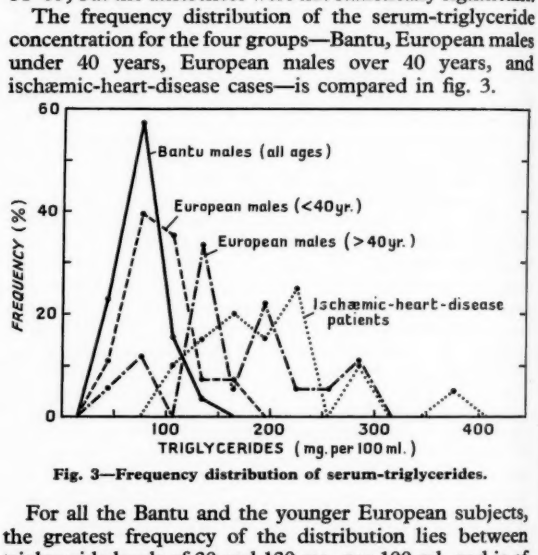

Fig. 3—Frequency distribution of serum-triglycerides.

For all the Bantu and the younger European subjects, the greatest frequency of the distribution lies between triglyceride levels of 30 and 130 mg. per 100 ml. and is of the " normal " type. Although just under 50% of the older European subjects and 25% of the heart-disease cases have serum-triglyceride levels within this range, the greater frequency distribution of these groups is at levels well over 150 mg. per 100 ml. The frequency distribution of the European female values (not shown in the figure) is almost identical with that of the Bantu.

Serum-triglyceride Polyenoic-fatty-acid Composition

The mean polyenoic-fatty-acid patterns of the subjects already described are shown in table II. Comparison of the pattern for the Bantu with those of the other subjects shows several differences.

As was the case for absolute serum-triglyceride levels, the polyenoic-fatty-acid distribution for Bantu, female Europeans, and heart-disease cases shows no variation with age, and the groups are considered homogeneous for statistical analysis. For male Europeans, however, a considerable inverse variation with age is shown in the percentage of dienoic fatty acids (linoleic acid)—this decreasing with increasing age. No significant changes are apparent for the more highly unsaturated polyenoic fatty acids. Ischæmic-heart-disease cases have a lower proportion of all polyenoic fatty acids in their serum-triglycerides than the other subjects.

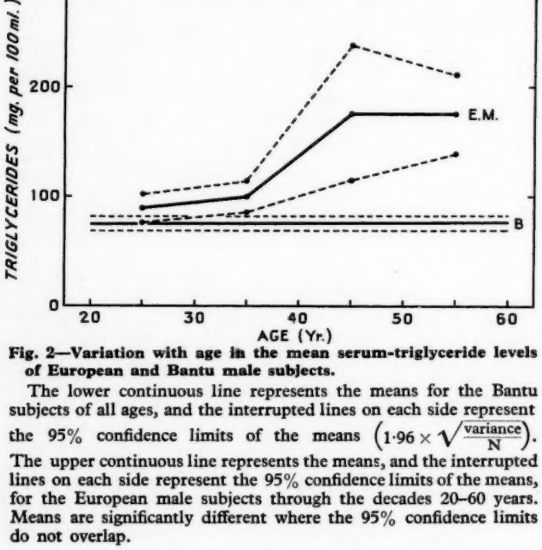

Fig. 2—Variation with age in the mean serum-triglyceride levels of European and Bantu male subjects.

The lower continuous line represents the means for the Bantu subjects of all ages, and the interrupted lines on each side represent the 95% confidence limits of the means $\left(1{\cdot}96\times\sqrt{\frac{\text{variance}}{N}}\right)$. The upper continuous line represents the means, and the interrupted lines on each side represent the 95% confidence limits of the means, for the European male subjects through the decades 20–60 years. Means are significantly different where the 95% confidence limits do not overlap.

Bantu serum-triglycerides have significantly greater proportions of dienoic, tetraenoic, and hexaenoic fatty acids than the corresponding serum-triglycerides of all the other groups. In comparison with European males under 30 years, values for P are less than 0·001, 0·01, and 0·01, respectively. European males under 30 years, and females under 46 years have triglyceride polyenoic-fatty-acid patterns not significantly different from each other, but both these patterns differ significantly in their dienoic-acid content from those of European males over 30 years and ischæmic-heart-disease cases ($0{\cdot}01 < P < 0{\cdot}02$).

Discussion

The statistical analysis of the age variation of the absolute serum-triglyceride levels of the European males reveals important aspects. Since not only the means for the different age-groups but also the standard deviations show significant variation, it seems apparent that the population is not homogeneous, and that different sections show different age trends. The under-30-year and the 31-40-year groups show only slight variation in the standard deviations of their mean serum-triglyceride concentration. For the older groups, however, the large and significant increase of the standard deviation suggests that there may be a mixture of two populations—one sample representing the true normals and showing a standard deviation possibly of the same order as the younger males, and a second sample representing subjects with a higher mean. The mean samples from the over-40-year groups would in this case be expected to show a biphasic frequency distribution. Although there is some indication that this may be the case (see fig. 3), the number of subjects investigated was too small to allow any firm conclusions to be drawn.

Since the mean level for the ischæmic-heart-disease patients was only slightly higher than that of the older European males, the implication could be that the older overtly normal population consists of a mixture of the true normals with a large proportion of subjects biochemically indistinguishable from ischæmic-heart-disease cases. These latter subjects may therefore represent potential cases of ischæmic heart-disease, and high serum-triglyceride levels may thus be predictive of future vascular disease. On the other hand the entire European male population as it ages may have a rising serum-triglyceride level without any distinct break between normals and abnormals; but in that event the rate of increase is not constant, the level rising more rapidly in some than in others.

Similar conclusions were reached by Albrink and Man (1959) in their study of an American population. They found that fasting serum-triglyceride levels exceeded 160 mg. per 100 ml. in only 5% of normal young adults, in 30% of normal men over 50 years, and in 90% of patients with ischæmic heart-disease. Our own study indicates a very much lower value for the upper limit of normal (114 mg. per 100 ml.), since 94% of the young European males, 97·5% of the Bantu males, and all the young European females have serum-triglyceride levels below this value. Possible objections to the use of the Bantu upper limit for both racial groups, on the grounds, firstly, of race difference and, secondly, that Bantu high-carbohydrate, low-fat dietary habits are very different from those of the European population, would not appear to be valid, since our own studies on a prison population (to be published shortly) have confirmed that both older European (aged 31–40 years) and Bantu prisoners who have subsisted for long periods on a prison diet almost identical in composition with that consumed by the urban Bantu population, have serum-triglyceride levels falling well within the upper limit of 114 mg. per 100 ml. In a given population irrespective of race, therefore, habituation to high-carbohydrate, low-fat calorie diets does not appear to lead to raised serum-triglyceride levels.

The Bantu and European subjects differed in their preparation in that the former were investigated after a day's work; but the influence of exercise on the fasting triglyceride levels, particularly in younger subjects, does not seem to be important since both the Bantu and European prisoners mentioned above had fasting levels, after a night's rest, not significantly different from those of the Bantu mineworkers. (For 26 European prisoners the mean was 83 ± 23, range 37–118, mg. per 100 ml.; and for 19 Bantu prisoners the mean was 86 ± 25 mg., range 46–121, mg. per 100 ml., with the exception of 1 Bantu volunteer whose fasting level varied between 136 and 158 mg. per 100 ml.)

It is nevertheless important, in evaluating serum-triglyceride levels, to consider the previous dietary history of the subjects, since restriction of dietary fat intake with isocaloric substitution by carbohydrate produces at once temporarily much-elevated triglyceride levels (Havel 1957a, 1957b, Albrink and Man 1956, Hatch et al. 1955, Ahrens et al. 1957, Ahrens 1957a, Ahrens et al. 1958, Kuo and Carson 1959, Dole et al. 1959). This could lead to incorrect interpretation of the basal fasting serum-triglyceride levels of individuals, especially since these raised levels appear to subside very slowly.

Comparison of the triglyceride levels with their polyenoic-fatty-acid composition indicates that raised levels are associated with a lowered proportion of dienoic acids. In the case of the Bantu the low serum-triglyceride levels are associated with significantly raised proportions of dienoic, tetraenoic, and hexaenoic fatty acids. Whether this finding represents a different fat metabolism in Bantu to that in the European subjects, or whether it is of dietary origin, is not clear. Recent studies by Ahrens et al. (1959), and by Dole et al. (1959) suggest that both factors are important. Ahrens et al. (1959) have shown that the composition of the serum-triglyceride fatty acids strikingly resembles the composition of the dietary fat, and we have confirmed this in our own studies. Dole et al. (1959), on the other hand, have shown that the immediate changes in serum-triglyceride fatty-acid composition produced by fat loading are slight, and have suggested that the fatty-acid pattern is more dependent on that of tissue-lipids. Since the composition of the latter, however, is also known to change gradually with the nature of the dietary fat over a long period, it seems that the changes in serum-triglyceride fatty-acid composition are secondary and depend on metabolic processes involving utilisation of depot fat.

The diet of the Bantu subjects is low in fat; but this is rich in linoleic acid, which has been shown to be a precursor for arachidonic and hexaenoic fatty-acid synthesis. This may partly account for the higher proportion of these polyenoic acids in the serum-triglycerides of the Bantu subjects than in those of the European subjects.

On the other hand, the diet of the European subjects in the present study is similar both in intake and in nature of the dietary fat (mainly saturated). The nature of the dietary fat therefore does not in this instance appear to be the only factor influencing the composition of the tri-

glyceride fatty acids, and the qualitative and quantitative variation of the serum-triglycerides in the European subjects may indicate a fundamental change in the triglyceride metabolism of the older European male compared with that of the younger European male and female and Bantu subjects. This change may be due to faults in fat transport and clearing mechanisms either produced or aggravated by excessive intake of dietary fats rich in saturated fatty acids. In view of the widely differing incidence of ischæmic heart-disease among these subjects—rare in the Bantu but becoming increasingly prevalent among younger European males—it would appear that ischæmic heart-disease, which is associated with raised serum-triglyceride levels, may also be largely due to faulty triglyceride metabolism brought about by habitual consumption of diets rich in saturated fat.

Long-term studies of triglyceride metabolism on normal subjects subsisting on such diets would give a clearer indication as to whether this possibly explains the raised serum-triglyceride levels of the older male population and the patients with heart-disease.

The influence of sex on serum-triglyceride composition and concentration are also apparently important since all the premenopausal females had low triglyceride levels. This corresponds to the lower prevalence of ischæmic heart-disease in premenopausal than in postmenopausal women.

Summary

The concentration and polyenoic-fatty-acid composition of serum-triglycerides has been estimated in 152 South African European and Bantu subjects, and in patients with ischæmic heart-disease.

Young European males, premenopausal European females, and Bantu males of all ages have similar, low, serum-triglyceride levels.

European males over 40 years of age, and patients with ischæmic heart-disease of all ages and each sex, have raised serum-triglyceride levels.

In European males a clear age trend is evident both in the polyenoic-fatty-acid composition and in the concentration of the serum-triglycerides. It is suggested that the older European male population consists of a mixture of " normals " and potential cases of ischæmic heart-disease, and that these two groups can possibly be distinguished by the serum-triglyceride levels.

We thank the Director of the South African Institute for Medical Research for his interest in this study; Miss C. D. Sussman, B.Sc., Miss C. Cavedoni, Miss E. Klinck, Mrs. A. Isaacs, and Mr. E. du Toit, B.Sc., for technical and other assistance; Dr. A. M. Adelstein for statistical analysis; and the volunteers who made this study possible.

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WEIGHT-LOSS IN PERNICIOUS ANÆMIA

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Thomas Addison, in his classical description of pernicious anæmia (1855), emphasised that patients with this disease remain obese. Today, the clinical impression is generally held that such patients do not lose weight, although there have been a few reports that some do.

Thus, Jones (1938) observed weight-loss in 42 of 78 patients with pernicious anæmia; while Read and Asher (1956) found weight-loss of over one stone in 14 out of 50 patients. On the other hand, Davis and Brown (1953) considered weight-loss to be rare in uncomplicated pernicious anæmia, and Girdwood and Innes (1958) note that these patients generally appeared well nourished.

When weight-loss is associated with alimentary symptoms the most likely diagnosis is often thought to be gastric carcinoma, although, in our experience, this combination of symptoms is not uncommon in pernicious anæmia. Consequently the simple diagnostic procedures which confirm the diagnosis of pernicious anæmia have sometimes been delayed, and in a few cases unnecessary laparotomies have been carried out. We therefore studied 50 cases of pernicious anæmia and 50 cases of gastric carcinoma in order to compare the clinical patterns of these two conditions. We were able to confirm that weight-loss occurred in a significant proportion of cases of pernicious anæmia. Since vitamin B_{12} is now known to influence the metabolism of many tissues besides blood we attempted at the same time to find out which tissues were mainly affected by the weight-loss associated with vitamin-B_{12} deprivation.

Materials and Methods

The 50 cases of pernicious anæmia and 50 cases of gastric carcinoma were admitted to the Western Infirmary in the two-year period 1957–58. The diagnosis of gastric carcinoma was accepted on the basis of laparotomy with biopsy and histological evidence. The criteria for acceptance of a diagnosis of pernicious anæmia were macrocytic anæmia, megaloblastic erythropoiesis in the bone-marrow, histamine-fast achlorhydria (Kay 1953), and a reticulocyte response of over 10% after treatment with vitamin B_{12}.

In 11 patients in whom we investigated weight-loss and red-blood-cell volume, serum-vitamin-B_{12} levels or vitamin-

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TABLE I—INCIDENCE OF PRINCIPAL CLINICAL FEATURES IN 50 CASES OF PERNICIOUS ANÆMIA AND 50 CASES OF GASTRIC CARCINOMA

Clinical features	Percentage of cases	
	Pernicious anæmia	Gastric carcinoma
Lack of energy	100	50
Pallor	100	54
Dyspnœa	76	24
Abdominal or dyspeptic symptoms	54	94
Anorexia	44	70
Loss of weight	36	42

B_{12}-absorption tests or both were done. In these 11 patients estimations of antipyrine space, thiocyanate space, and plasma-volume (Evans-blue) were carried out before treatment and at least three months later by the methods described by Muldowney (1957). It was found that within three months the blood values and the weights of the patients had been restored to their normal levels. "Lean body mass" was calculated from the antipyrine space by the equation of Pace and Rathbun (1945) and in addition by the Keys-Brozek formula (Keys and Brozek 1953), which takes into account the extracellular fluid as deduced from the thiocyanate space.

Results

Lack of energy, pallor, and dyspnœa were the commonest features of pernicious anæmia; while abdominal or dyspeptic symptoms, anorexia, and loss of weight were the commonest in gastric carcinoma (table I).

We have described epigastric pain or discomfort, heartburn, sour mouthfuls, flatulence, nausea, vomiting, or diarrhœa as "abdominal or dyspeptic symptoms". "Loss of weight" indicates an estimated weight-loss of 14 lb. or more in the year preceding diagnosis. 36% of our patients with pernicious anæmia had a weight-loss of 14 lb. or more. The results of analysis of some laboratory investigations are recorded in table II. Anæmia in gastric carcinoma can be as severe as that in pernicious anæmia, but is not usually so. The erythrocyte-sedimentation rate (Westergren) varied from normal to much increased in each disease. On the other hand the fæcal occult-blood test was positive in only 4 of 37 cases of pernicious anæmia but was positive in 9 out of 12 cases of gastric carcinoma so tested. Histamine-fast achlorhydria was found in all cases tested in each disease, but only 13 such investigations were recorded in the cases of gastric carcinoma. Clearly there is much overlap in the clinical features of these two diseases, which may explain the fact that 11 patients (22%) with pernicious anæmia were initially suspected of having gastric carcinoma. 5 were referred initially to surgeons because of severe alimentary symptoms associated with weight-loss, and 3 of these were admitted to surgical wards; 1 patient was further investigated by means of gastroscopy. Physicians made the initial diagnosis of gastric carcinoma in 6 cases which were later shown to be of pernicious anæmia; in each of these cases weight-loss was a prominent clinical feature.

TABLE II—RESULTS OF LABORATORY INVESTIGATIONS IN PERNICIOUS ANÆMIA AND GASTRIC CARCINOMA (NUMBER OF CASES INVESTIGATED SHOWN IN PARENTHESES)

—	Pernicious anæmia	Gastric carcinoma
Hb (%):		
Range	23–66 (50)	26–107 (32)
Mean and S.D.	44±11 (50)	70±19 (32)
E.S.R.	5–116 (37)	4–45 (22)
F.O.B. positive	4 (37)	9 (12)
H.F.A.	50 (50)	13 (13)

Hæmoglobin (Hb) 100% = 14·8 g. per 100 ml.
S.D. = standard deviation.
E.S.R. = erythrocyte-sedimentation rate (Westergren) mm. in first hour.
F.O.B. = fæcal occult blood.
H.F.A. = histamine-fast achlorhydria.

Muldowney (1957) showed that for normal people the red-blood-cell volume did not closely correlate with the total body-weight. He did find, however, close correlation between red-cell volume and "lean body mass" in normal people, and the linear regression of red-cell volume (y) on "lean body mass" (x) was found to be $y = 32{\cdot}7x + 155{\cdot}17$. In our patients with untreated pernicious anæmia the (product moment) coefficient of correlation between red-cell volume and total body-weight was +0·41, which is not significantly different from zero; in treated cases the coefficient of correlation was +0·64 which is significantly different from zero ($P < 0{\cdot}05$). In our 11 untreated cases of pernicious anæmia the correlation coefficient between red-cell volume and "lean body mass" was +0·36, which is not significantly different from zero. For the treated state the corresponding coefficient of correlation was +0·92, which is significantly different from zero ($P < 0{\cdot}01$). This is illustrated in fig. 1. The linear regression of red-cell volume (y) on "lean body mass" (x) was found to be $y = 31{\cdot}70x + 277{\cdot}3$. The regression coefficient (31·70) agrees very satisfactorily with Muldowney's value of 32·74.

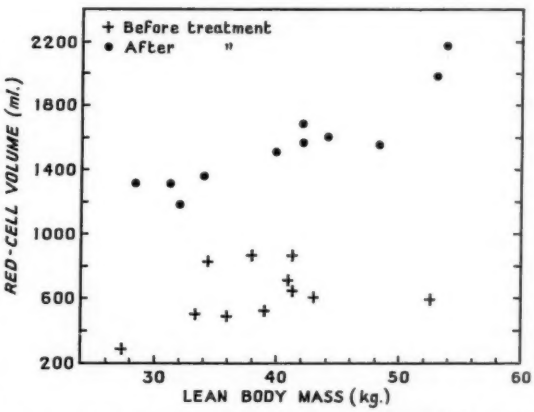

Fig. 1—Scatter diagram of red-cell volume and "lean body mass" in patients with pernicious anæmia before and after treatment.

The gain in weight of these 11 patients after the restoration of normal blood-levels varied from under 5 kg. to over 15 kg. The measurement of "lean body mass" allowed us to estimate that proportion of weight gain due to fat and that due to lean tissue (table III). The estimation of "lean body mass" derived from the antipyrine space by the Pace-Rathbun equation was compared with that derived from the Keys-Brozek formula which incorporates a correction for extracellular-fluid changes. The mean difference between the two estimations (Pace-Rathbun minus Keys-Brozek) for the 11 untreated patients was only +0·06 kg., and for the patients after treatment it was only −0·12 kg. This suggests that the estimations of "lean body mass" were valid despite the possibility of subclinical œdema in untreated patients with pernicious anæmia. In only 1 of these patients (case 4) was there any evidence of clinical œdema, and this was mild. In this patient the measurement of extracellular fluid by thiocyanate was significantly

TABLE III—COMPARISON OF WEIGHT, "LEAN BODY MASS" (L.B.M.) TOTAL FAT, RED-CELL VOLUME, AND THIOCYANATE (EXTRACELLULAR-FLUID) SPACE IN 11 CASES OF PERNICIOUS ANÆMIA, BEFORE AND AFTER TREATMENT WITH VITAMIN B_{12}

Case no.	Body-weight (kg.)		Pace-Rathbun				Keys-Brozek				Red-cell vol. (ml.)		Thiocyanate space (litres)	
			L.B.M. (kg.)		Fat (kg.)		L.B.M. (kg.)		Fat (kg.)					
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
1	75·0	87·7	52·4	53·9	22·6	33·8	52·89	54·55	22·11	32·15	590	2166	17·50	17·70
2	65·9	69·5	41·2	41·8	24·7	27·7	42·32	42·86	23·08	26·64	656	1695	12·00	12·20
3	44·9	56·8	27·2	28·4	17·7	28·4	26·87	29·28	18·03	26·52	283	1308	10·75	8·70
4	63·6	70·0	37·9	33·8	25·7	36·2	35·57	32·36	27·43	37·64	867	1374	19·60	12·88
5	61·4	67·3	34·4	31·3	27·0	36·0	32·80	28·90	28·60	38·40	817	1300	11·40	12·00
6	50·9	54·1	33·3	32·2	17·6	21·9	33·57	31·96	17·32	22·14	508	1169	11·20	12·10
7	51·8	67·3	36·2	39·5	15·6	27·8	36·47	39·60	15·33	27·70	497	1517	12·30	13·90
8	52·7	66·4	43·0	52·9	9·7	13·5	42·61	52·72	10·09	13·68	612	1999	16·40	19·40
9	45·0	48·6	41·0	43·9	4·0	4·7	41·63	44·17	3·37	3·43	704	1560	13·10	12·50
10	45·0	59·5	38·9	41·9	6·1	17·6	39·76	42·66	5·24	16·84	520	1578	11·75	13·12
11	53·6	63·2	41·2	48·2	12·4	15·0	41·41	49·85	12·19	13·35	863	1580	14·32	13·10

changed following treatment with vitamin B_{12}. From these studies it would appear that the fatter patients gained either wholly or mainly fat, while the lean patients gained predominantly lean tissue (fig. 2).

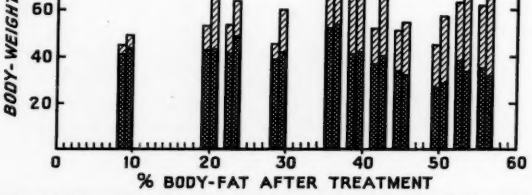

Fig. 2—Proportions of fat and lean tissue in 11 patients with pernicious anæmia.
Each two adjacent columns represent these tissue proportions in a patient before treatment (left column) and after treatment (right column). The columns are placed on the abscissa according to their approximate body-fat content after treatment.

Discussion

The results of our clinical analysis have indicated the many features which are shared by pernicious anæmia and gastric carcinoma. Unless it is appreciated that a patient with pernicious anæmia may have considerable loss of weight, dyspeptic symptoms, an increased erythrocyte-sedimentation rate, and more rarely a positive test for fæcal occult blood, much effort may be misdirected and much time lost in coming to the correct diagnosis. The increased incidence of gastric carcinoma in patients with pernicious anæmia (Mosbech and Videbach 1950) must not be forgotten. Nevertheless, if further investigations are necessary to eliminate this possibility, these can be carried out after the patient has been treated.

The highly significant coefficient of correlation (+0·92) between red-cell volume and "lean body mass" found in treated patients has confirmed Muldowney's results in normal subjects. The estimations of weight-gain after treatment demonstrated a predominant accumulation of fat in obese patients and an accumulation mainly of lean tissue in lean patients. In general, all these patients returned to their usual weight, and so it can reasonably be assumed that the measurements of lean and fat tissue gained were, in fact, indicative of the proportions of these tissues lost as a result of vitamin-B_{12} deprivation. Vitamin B_{12} has been shown to influence the metabolism of protein, nucleic acids, carbohydrate, and fat (Arnstein 1955) in addition to its well-known effect on blood and nervous tissue.

In pernicious anæmia the dramatic clinical feature is usually a diminution of circulating hæmoglobin. The more subtle changes in other tissues become apparent soon after treatment is initiated by the patient's remarkable feeling of well-being long before the mass of circulating hæmoglobin is significantly altered. Weight-loss is another manifestation of this tissue dependence on vitamin B_{12}. Although some of this weight-loss can be attributed to anorexia, a more direct cause may be the depletion of vitamin B_{12} throughout the tissues of the body.

Summary

Of 50 consecutive cases of pernicious anæmia admitted to the Western Infirmary, Glasgow, 18 (36%) had an estimated weight-loss of at least 14 lb. over a period of less than a year preceding diagnosis.

In cases with weight-loss and alimentary symptoms, the diagnosis may be confused with that of gastric carcinoma. For this reason the main clinical features of 50 cases of gastric carcinoma were compared with those of the 50 cases of pernicious anæmia. There is considerable overlap of these features in the two diseases.

11 patients with pernicious anæmia who had lost weight had the "lean body mass" estimated before and after treatment. These studies showed that, whereas obese patients tend to lose fat and lean patients lean tissue, both may be lost in some cases.

The normal correlation between red-cell volume and lean body mass is greatly disturbed in the untreated state, but is restored after treatment.

We are grateful to Prof. E. J. Wayne and Dr. J. A. W. McCluskie in whose wards we carried out these studies; to physicians and surgeons in the Western Infirmary, Glasgow, who allowed us access to their case-records; to Miss E. Macdonald, B.SC., who performed the estimations of antipyrine and thiocyanate; to Dr. R. A. Robb, Mitchell lecturer in statistics, University of Glasgow, for the statistical analysis; and to Dr. J. F. Adams who kindly carried out the serum-vitamin-B_{12} assays and the vitamin-B_{12}-absorption tests.

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FLACCID QUADRIPLEGIA FOLLOWING URETERIC TRANSPLANT

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ANASTOMOSIS of the ureter to the colon often produces metabolic abnormalities (Wilkinson 1954, Milne 1957). These were present in 80% of patients a year after operation (Ferris and Odel 1950), and consisted of a raised blood-urea and plasma-chloride with a lowered plasma-bicarbonate. Significant hypokalæmia has been reported in 35% of cases (Jacobs and Stirling 1952), occasionally being severe (Parsons et al. 1952, Wilkinson 1952). These biochemical abnormalities did not invariably cause symptoms; if present these consisted of tiredness, weakness, anorexia, nausea and vomiting, a salty taste in the mouth, and thirst and consequent polyuria (Milne 1957).

Hypokalæmia has been associated with muscular weakness (Foster et al. 1950, Matern 1954); and Diefenbach et al. (1951), Skanse and Widén (1955), and Loughlin (1956) have described cases in which flaccid quadriplegia developed, as in the case reported here.

DATA ON BLOOD CHEMISTRY IN THE FIRST FOUR DAYS AFTER ADMISSION AND SIX MONTHS LATER

—	Oct. 7, 1958	Oct. 8, 1958	Oct. 9, 1958	Oct. 10, 1958	April 6, 1959
Plasma-sodium (mEq. per litre)	135	143	139	144	142
Plasma-potassium (mEq. per litre)	1·5	2·8	3·5	4·5	4·2
Plasma-chloride (mEq. per litre)	114	100	95	98	111
Plasma alkali reserve (mM. per litre)	12	23	33	37	17
Blood-urea (mg. per 100 ml.)	100	70	45	45	80

Case-report

A male clerk, aged 25, was admitted to hospital on Oct. 6, 1958, with a provisional diagnosis of acute poliomyelitis. For some days he had felt thirsty, with a dry throat, and two days previously he had felt tired after a strenuous game of football; the next day he had felt weak and noticed " a heaviness in the legs ". On the day of admission he found it impossible to go to work owing to weakness of his arms and legs, and that evening he was found to have severe weakness of the proximal muscle-groups of all four limbs. The reflexes were all present and sensation was normal. His temperature was 98·4°F, pulse-rate 70 per minute, respiration-rate 20 per minute. During the night he vomited repeatedly, and when seen the following morning he was dehydrated and clinically uræmic. The paralysis had progressed; he was unable to move any of his limbs, nor could he raise his head from the pillow. Respiration was rapid and shallow, and he could count only to ten in one breath.

There was a past history of left-sided nephrectomy in 1946, on account of renal tuberculosis. In 1949 the right ureter was transplanted into the sigmoid colon owing to pronounced frequency of micturition, the bladder capacity being only 2 oz. Since the last operation he had been continent of urine and normally emptied his bowel every three hours. About eight years previously he had had an attack of weakness of the limbs lasting several days which was associated with vomiting and constipation, and which responded to the administration of purgatives. In April, 1957, he was treated in hospital for an attack of acute pyelonephritis, and subsequently intravenous pyelography showed a satisfactorily functioning large right kidney with slight dilatation of the calyces. Apart from these episodes he had remained generally well and played football regularly at the weekends.

Flaccid quadriplegia due to hypokalæmia was diagnosed clinically. Estimation of plasma-electrolytes (see table) revealed a plasma-potassium of 1·5 mEq. per litre. Electrocardiography (see figure) showed the changes of severe hypokalæmia (Surawicz et al. 1957). The hæmoglobin was 132% (19·6 g. per 100 ml.), packed-cell volume 57%, white blood-cells 15,000 per c.mm. (polymorphs 90%).

Treatment and Progress

Intravenous therapy was started, and during the next twenty-four hours the patient received 3 litres of a solution containing 0·18% sodium chloride, 4·3% dextrose, and 0·1% potassium chloride and 3 litres of 1·87% sodium lactate. In addition he was able to take copious fluids by mouth and mist pot. cit. *B.P.C.* 1/2 oz. four-hourly. A rectal tube was inserted so that urine could be drained off continuously, and intramuscular streptomycin g. 1 b.d. was given for the next five days in case of urinary infection.

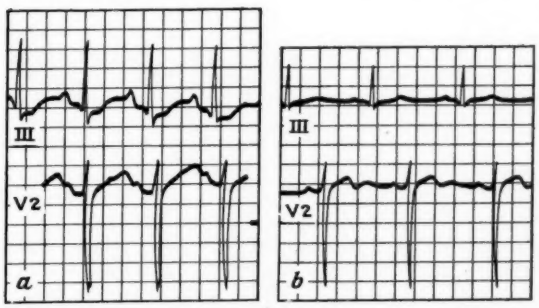
By the next morning the patient's condition was greatly improved. He was obviously less dehydrated and could move his arms and legs, but he was still unable to raise his head from the pillow. The blood chemistry showed improvement (see table, Oct. 8). Intravenous therapy was stopped, but mist pot. cit. *B.P.C.* and fluids were continued by mouth, salt being restricted. The rectal drainage tube was removed after forty-eight hours. He continued to improve symptomatically, and the plasma-potassium rose progressively to 4·5 mEq. per litre on Oct. 10 (see table). The electrocardiogram had become normal (see figure, *b*).

The patient was discharged from hospital on Oct. 14, 1958, feeling very well and taking a normal diet with no salt restriction. He was given mist pot. cit. *B.P.C.* 1/2 oz. b.d. and was advised to increase the dosage if any muscular weakness developed. He was instructed to pass urine at intervals of not more than three hours. Since discharge he has attended as an outpatient. He has remained well, playing football at weekends, and continues on potassium citrate regularly.

The latest blood-chemistry findings (April 6, 1959) showed hyperchloræmic acidosis with raised blood-urea but normal potassium (see table).

Discussion

After ureterosigmoidostomy reabsorption of urea from the urine in the bowel results in a raised blood-urea which does not necessarily imply renal dysfunction. Similarly, reabsorption of chloride ions by the colon preferentially to sodium ions accounts for the hyperchloræmic acidosis (Parsons et al. 1952). Electrolyte disturbances are more severe when the ureters are transplanted into the cæcum



Electrocardiograms (leads III and V_2): *a*, Oct. 7, 1958, showing sinus rhythm, PR interval 0·20 sec., QRS 0·12 sec., tall tilted P waves depressed ST segments, marked U waves which are taller than T waves in V_2 (plasma-potassium 1·5 mEq. per litre); *b*, Oct. 9, 1958, normal appearance, with sinus rhythm, PR interval 0·18 sec., QRS 0·1 sec. (plasma-potassium 3·5 mEq. per litre).

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or proximal colon than when they are transplanted into the sigmoid colon. This has been demonstrated in animal experiments, in which the lower the level of the colon at which the ureteric transplant was inserted the lower was the mortality-rate (Boyce 1951). Similarly, in man there has been a higher mortality where the right ureter has been anastomosed to the cæcum and the left to the sigmoid colon (Kekwick et al. 1951). These biochemical abnormalities may exist where renal function has been normal (Mitchell and Valk 1953).

Hypokalæmia, though less common than other electrolyte disturbances, may have more serious consequences. Its precise causation is not fully understood; but it is thought to result partly from renal tubular dysfunction. This may result from chronic pyelonephritis, which is almost invariably present in cases coming to necropsy (Graves and Buddington 1950). In addition, because of the excessive absorption of chloride, sodium, and urea from the bowel, there is obligatory osmotic diuresis resulting in loss of potassium (Stamey 1956). Apart from the renal factors, potassium may be lost into the colonic contents from the mucosa of the bowel (Parsons et al. 1952, Stamey 1956). Potassium deficiency may cause weakness of voluntary muscles, progressing in extreme cases to flaccid quadriplegia, as in the present case.

In cases of ureterosigmoidostomy, both doctors and patients should be aware of the possibility of serious electrolyte disturbances. These are especially likely during an illness in which there is vomiting or diarrhœa, following excessive perspiration, or if constipation develops.

As a prophylactic measure these patients should be instructed to evacuate the bowel of urine at intervals of three hours or less, they should ensure an adequate fluid intake, and it may be necessary to give regular supplements of alkali and potassium. If they begin to feel weak or lethargic, electrolyte control will be required; and treatment should be aimed at correcting the metabolic abnormalities.

Summary

Flaccid quadriplegia due to hypokalæmia developed in a patient nine years after ureterosigmoidostomy. The patient presented with paralysis which was thought at first to be due to acute poliomyelitis, but which responded dramatically to correction of the metabolic abnormalities.

Patients and doctors should be aware that preventable complications may follow this type of operation.

We wish to thank Dr. K. O. Rawlings for permission to publish this case and for helpful advice and criticism.

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Addendum

Since this paper was completed, K. G. Lowe, J. M. Stowers, and W. F. Walker (*Scot. med. J.* 1959, **4**, 473) have described two cases of paralysis due to hypokalæmia —in one eleven years and in the other four years after ureterosigmoidostomy. A. W. Steinbeck and J. H. Tyrer (*Brit. J. Urol.* 1959, **31**, 280) have reported the case of a man who had his first attack of paralysis twenty years after ureterosigmoidostomy and in the next five years had about a hundred similar episodes; since sodium citrate and potassium citrate have been given daily, there has been no further paralysis. R. A. Straffon and A. J. Coppridge (*J. Amer. med. Ass.* 1959, **171**, 139) have described two cases which presented with flaccid quadriplegia and with respiratory paralysis requiring treatment in a tank respirator. Acute poliomyelitis and Landry's acute ascending paralysis had been provisionally diagnosed. When investigations revealed severe hypokalæmia (ureterosigmoidostomy had been performed on both, six years and fourteen years before) treatment with potassium was started. The response to treatment was dramatic, one patient being removed from the respirator within a matter of hours and the other by the next day.

BROKEN TRACHEOTOMY TUBE AS A FOREIGN BODY

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SINCE tracheotomy became common in the treatment of respiratory poliomyelitis, and particularly since positive-pressure respiration was introduced,[1–3] many patients have had to wear tracheotomy tubes over long periods. We describe here an accident to one such patient, arising from causes of which we were not at that time aware.

The patient, a farmer's wife aged 35, was admitted to the department on Aug. 17, 1958, with poliomyelitis. During the first 24 hours severe paralysis of the trunk and extremities developed, and signs of bulbar involvement. Tracheotomy was necessary, and the respiratory muscles remained paralysed. Respiration was maintained by the Engstrøm respirator, the Kifa cuirass respirator, and a rocking bed.

On Feb. 17, 1959, some respiratory infection was noticed. There were signs of bronchitis, especially in the right lung, and a purulent discharge from the cannula. When the cannula was changed, a large defect was found in it (fig. 1), and an X-ray of

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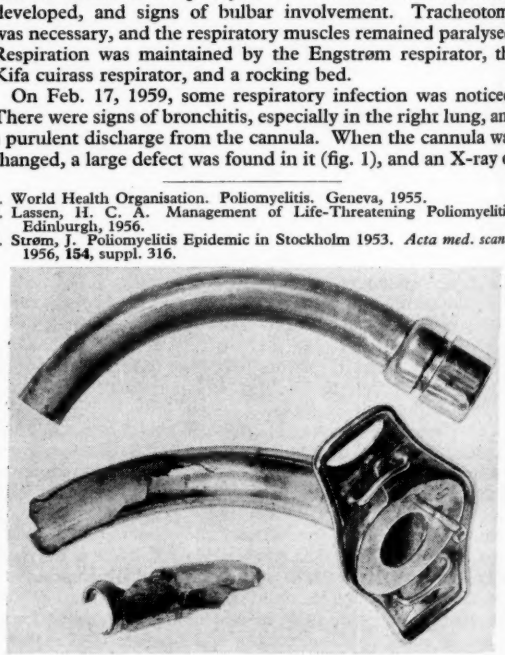

Fig. 1—The broken tracheotomy tube.

the lungs showed a fragment in the right main bronchus (fig. 2). Bronchoscopy was performed and the foreign body was removed. The patient is still wearing a cannula and must be regarded as a chronic respiratory case.

The cannula removed from this patient showed obvious cracks on the outer surface, although the inner part looked intact. We then examined all the cannulas in the department, and found 3 more which appeared faulty and on closer examination were seen to have cracks. These cannulas were sent to the Oslo Material - Testing Station for investigation. They were made of german silver, containing 18% nickel (the maker's statement). Magnification 40 times showed cracks in the alloy. The split formation was caused by "season cracking" (splitting caused by long-continued high internal stresses in the surface and the action of a relatively weak corroding medium, usually one or other of the quaternary ammonium compounds). Fig. 3 shows a photomicrograph ×360 of the numerous transcrystalline cracks.

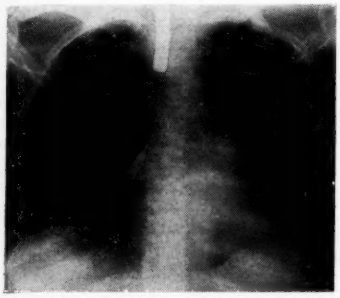

Fig. 2—X-ray of the lungs showing foreign body in the right main bronchus.

The most remarkable thing about this damaged cannula was the widespread splitting, and it might have broken into several pieces. The cracks could not be seen by the naked eye, but required a magnification of ×30 for their detection. Straight transcrystalline splitting indicates "corrosion fatigue" in the metal: this usually occurs when the metal is subjected to changing stresses, particularly in the presence of a corrosive. This cannula was not subjected to mechanical stresses, and the split was probably caused by inner stress in the material from damage to the nickel coating. In some cases (though not in ours) the bronchial secretion is alkaline.

For many years, this department, besides using silver cannulas specially made to fit the respirator, has also used cannulas of german silver, because these are cheaper and can be thrown away as soon as they show signs of wear. The routine for patients who have to stay long in a respirator is to change the cannula every 10–14 days.

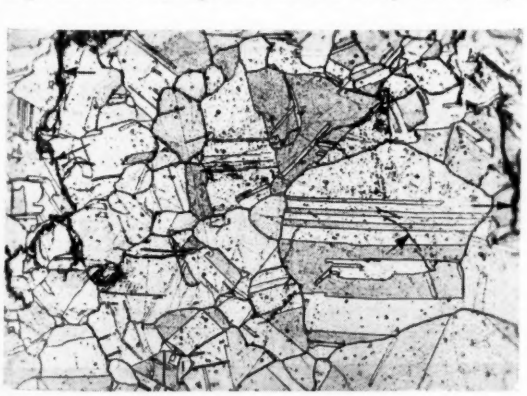

Fig. 3—Photomicrograph of the cannula showing numerous transcrystalline cracks (×360).

In many parts of Norway the cannulas made of german silver are commonly called "silver cannulas". After this accident we shall in future use only pure silver cannulas, though these, being softer than german silver, will wear out sooner.

Summary

Respiratory infection in a patient with poliomyelitis was found to be due to breakage of the tracheotomy cannula, part of which was found as a foreign body in the right main bronchus. When put in place 14 days earlier it had appeared free from fault. It was of german silver and the cause of the break was "season cracking". In chronic respiratory cases only pure silver cannulas should be used.

Preliminary Communication

A NEW DIAGNOSTIC TEST IN AMYLOIDOSIS

SINCE it was introduced in 1923 by Bennhold,[1] the congo-red test has been widely used to establish the presence of amyloidosis. However, no full agreement exists over the evaluation of the test. Some workers consider that if more than 60% of the dye disappears from the blood within 45 minutes of intravenous injection, this may be taken as a sign of amyloidosis, but others [2 3] maintain that only a complete (99–100%) removal is conclusive.

Side-effects are rare, but may occur. In this department a patient who had an intravenous injection of congo red immediately showed a severe allergic reaction with dyspnœa, œdema of the face and larynx, and circulatory collapse. He recovered.

PRESENT INVESTIGATION

Patient A, with primary amyloidosis (confirmed by needle biopsy of the liver) and hypoalbuminæmia had ^{131}I-polyvinylpyrrolidone (^{131}I-P.V.P.)[4] administered intravenously to rule out intestinal protein leakage caused by intestinal amyloidosis. As part of the investigation he had Evans blue *U.S.P.* intravenously at the same time. 15 minutes later blood was withdrawn for determination of dye concentration[5] and radioactivity. The initial distribution-volume of Evans blue is supposed to be identical with plasma-volume; and, whereas in all the other patients (about 60) examined until then, it had been lower than the distribution-volume of ^{131}I-P.V.P. (usually by 15–50%), in this patient it was 10% higher.

To confirm this finding, Evans blue and human serum-albumin, labelled with radioactive iodine, were injected simultaneously and the concentrations determined in plasma 15 and 45 minutes after the injection. The 15-minute concentration was used to calculate plasma-volume. Normally, the plasma-volume as determined with Evans blue ($P.V._E$) or with ^{131}I-albumin ($P.V._A$) are identical,[5–7] and the disappearance-rate does not differ within the first hour after injection, amounting to 6–12% per hour.[8] However, in the patient with amyloidosis $P.V._E$ (4600 ml.) exceeded $P.V._A$ (3150 ml.) by 46%. The disappearance-rate of Evans blue within the first hour was appreciably higher than that of ^{131}I-albumin as shown in fig. 1.

45 minutes after injection the ^{131}I-albumin concentration had decreased by 7%, and that of Evans blue by 30%, compared with the concentration 15 minutes after injection. The

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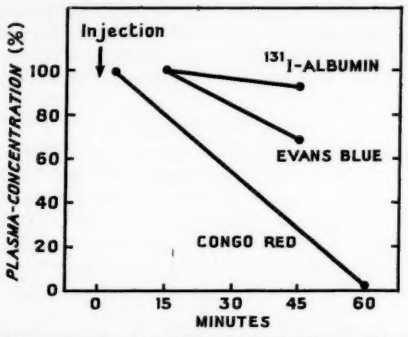


Fig. 1—Disappearance-rate in blood of ^{131}I-albumin, Evans blue, and congo red in a patient with primary amyloidosis.

The highest concentration measured is given an arbitrary value of 100.

congo-red test was positive, 99% being removed from the blood in the interval 4 to 45 minutes after injection.

With this new knowledge an old mystery was solved.

9 months earlier a marked discrepancy between P.V.$_E$ and P.V.$_A$ had been found in patient B, extremely ill with ulcerative colitis and osteoarthritic spondylitis. Investigation with ^{131}I-albumin had been undertaken, and to check that he remained in a steady state, P.V.$_E$ was determined at 3-day intervals. The anomalous results are recorded in the table (patient B).

First P.V.$_E$ was nearly 3 times higher than P.V.$_A$: subsequently P.V.$_E$ decreased, suggesting that a certain saturation of the Evans blue binding-system had taken place.

The patient had part of his colon resected, but died a few weeks later. The only noteworthy macroscopical finding at necropsy was a big liver. Microscopically, however, extensive amyloidosis was seen in the liver, spleen, and kidneys.

PLASMA-VOLUMES AS DETERMINED BY ^{131}I-ALBUMIN AND EVANS BLUE IN 3 PATIENTS WITH AMYLOIDOSIS AND 1 WITH MYELOMATOSIS.

Patient	Age and sex	Diagnosis	Date	Plasma-volume		Serum γ-globulin (g. per 100 ml.)
				Iodised albumin (ml.)	Evans blue (ml.)	
A	42 M	Primary amyloidosis ..	Jan. 5	3150	4600	0·99
B	32 M	Ulcerative colitis; osteoarthritic spondylitis; secondary amyloidosis	April 13 „ 17 „ 20 „ 23	3200	.. 9430 6710 5910	2·03 .. .. ..
C	40 F	Myelomatosis; secondary amyloidosis ..	Feb. 24	4670	14,400	0·97
D	73 M	Myelomatosis..	Feb. 20	3290	3260	8·09

A third patient (C) with myelomatosis and secondary amyloidosis, confirmed by liver biopsy, received simultaneous intravenous injections of Evans blue and ^{131}I-albumin. Blood samples were withdrawn after 4, 8, 15, and 45 minutes. The results are shown in fig. 2.

The plasma concentration of Evans blue falls rapidly within the first 15 minutes and then more slowly, while the ^{131}I-albumin concentration shows a linear and slow decline like Evans blue in a normal person (top curve). The different disappearance-rate of Evans blue and ^{131}I-albumin is obvious 15 minutes after injection, when the dye concentration is 42% less than that of the 4-minute sample. In this patient P.V.$_E$ (14,400 ml.) exceeded P.V.$_A$ (4670 ml.) by 208% (see table, patient C). The congo red test was positive. The patient cleared her blood completely of congo red within 60 minutes.

DISCUSSION

This finding that Evans blue is removed from plasma much faster in amyloidosis than in any other state, and to such a degree that plasma-volume determined with Evans blue from a 15-minute sample may be more than 200% too high, has not been described before.

Verel [9] in a series of 38 patients suffering from a variety of diseases found the ratio body/venous hæmatocrit as determined by Evans blue and ^{51}Cr-erythrocytes to be lowest (0·79) in a case of amyloidosis. This may be a falsely low value due to an erroneously high P.V.$_E$.

A diagnostic test could be based on these findings, and I would suggest one of the following two procedures:

1. Blood samples are taken 4 (A) and 15 (B) minutes after the injection of a known amount of Evans blue. If the dye-concentration of B is less than 80% of A, amyloidosis is probable.

2. If equipment for radioactive measurements is at hand this test may be combined with a better one. Known amounts of Evans blue and ^{131}I-albumin are injected immediately after each other (but not in the same syringe [10]). 15 minutes later blood is withdrawn, and distribution-volumes are determined. If P.V.$_E$ exceeds P.V.$_A$ by more than 10%, the patient probably has amyloidosis.

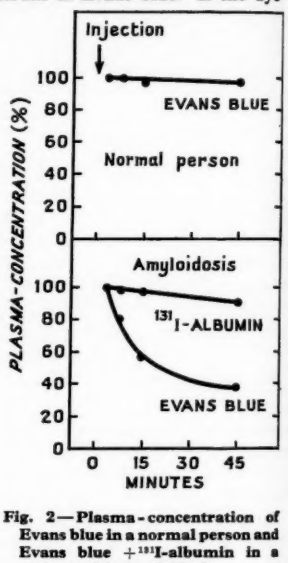


Fig. 2—Plasma-concentration of Evans blue in a normal person and Evans blue + ^{131}I-albumin in a patient with amyloidosis.

Concentration is given as a percentage of the concentration 4 minutes after injection.

These tests may turn out to be more specific than the congo-red test, as the rapid removal of Evans blue can only be due to an abnormal non-circulating protein with a dye-binding power, which is many times that of the ordinary plasma globulins and perhaps nearly as high as that of albumin. The abnormal protein could be in or close to the capillary wall. Were it intravascular it would not affect determination of plasma-volume with Evans blue. In a case of myelomatosis with a high concentration in the plasma of an abnormal gamma-globulin, the P.V.$_E$ was correct (see table, patient D).

SUMMARY

The dye Evans blue, extensively used for plasma-volume determination, is removed at an abnormally high rate from the blood in patients suffering from amyloidosis. Therefore it cannot be used for plasma-volume determinations in this disease. On the other hand it can be of diagnostic value, and two new diagnostic tests using Evans blue are suggested for confirming the presence of amyloidosis.

I wish to thank Prof. H. C. Gram, Sundby Hospital, for kind permission to examine one of the patients with amyloidosis. This work was supported by grants from King Christian X's Fund.

Department of Clinical Biochemistry and Medical Department B, Bispebjerg Hospital, Copenhagen

STIG JARNUM
M.D. Copenhagen

9. Verel, D. *Clin. Sci.* 1954, **13**, 51.
10. Freinkel, N., Schreiner, G. E., Athens, J. W., Hiatt, C. W., Breese, S. *J. Lab. clin. Med.* 1954, **43**, 215.

Medical Societies

ASSOCIATION OF CLINICAL PATHOLOGISTS

THE 64th general meeting of the Association was held in Cardiff, on April 7–9. We publish below a brief account of some of the contributions.

Cross-infection in Hospital

Prof. S. D. ELEK and Dr. P. C. FLEMING (St. George's Hospital) had made use of Gould's observation that in hospitals there was a detectable amount of penicillin floating in the air, causing selective exclusion of penicillin-sensitive staphylococci from the noses of those in hospital. They aimed to eliminate nasal carriage with a new experimental antibiotic (AB1241) which fulfilled the following requirements: (1) it was active against all of 400 strains of *Staphylococcos pyogenes* tested; (2) it was active in concentrations of 1–5 μg. per ml. and highly bactericidal at about the bacteriostatic level; (3) resistance could not be induced in 12 strains by 20 serial passages through Szybalski gradient plates. The substance was odourless and non-irritant. A maternity unit was chosen for the spraying experiment because of the known high incidence of nasal carriage in infants. Approximately 55% of daily nasal swabs taken from each of 58 newborn infants during their first ten days grew pyogenic staphylococci. Daily spraying of 1 g. of the drug was next carried out in one ward and nursery occupying about 15,000 c. ft. using a commercial window-cleaning sprayer. This halved the nasal carriage but failed to abolish it. Increasing the concentration to 1 g. 4 times a day led to further reduction for the next 20 babies. Thereafter a cumulative effect became manifest as the drug began to build up in the environment. No pyogenic staphylococci at all were isolated from the next 24 babies during their ten days in hospital. No resistant strains emerged, and no hypersensitivity phenomena were observed over the twenty weeks. This seemed to be a simple and effective means of eliminating nasal carriage in babies and was put forward as a possible approach for the control of wound sepsis in hospitals.

Dr. BERYL CORNER and Dr. W. A. GILLESPIE (Bristol) showed that the spread of staphylococcal infection in maternity hospitals was quite rapid once there was an accumulation of resistant strains. The ordinary accepted methods of interrupting spread were disappointing in the long run. The infection arose from adult carriers and was spread superficially by nose and skin, particularly the umbilicus. By the continuous use of hexachloraphate powder and by the instillation of chlorhexidine ('Hibitane') and neomycin in the noses of mothers and babies there was a striking reduction in the staphylococcal rate in both mothers and babies—particularly in the follow-up clinics in the incidence of breast abscesses, and sticky eyes in the children. It was evident, however, in the most recent survey that monilia were now taking a firmer hold in the wards, and in the last bacterial survey there were 25 cases of spots due to staphylococci, 3 streptococcal abscesses, and 72 cases of monilial infection.

The Hospital Vacuum Cleaner

Dr. J. G. BATE (Princess Louise Hospital) described how the bacterial content of the air from ten vacuum cleaners and three suction polishers in use in hospital wards was investigated. Bacteria-carrying particles were counted by a slit-sampler operating inside a large polyethylene reservoir in which stationary samples of exhaust air were collected from a polyethylene wind-tunnel in which the cleaners were operated. Serial samples of 5 c. ft. were collected from machines before and after a thirty-minute continuous run during which the airflow was regularly interrupted every fifteen seconds in order to stress the filters. With one exception the vacuum cleaners gave colony counts not exceeding 2 in 10 c. ft. and retained not less than 97% of the number of airborne bacteria found in the room air immediately before the test. One machine consistently gave counts of up to 5 colonies, retaining only 90% of the aspirated organisms. Suction polishers gave counts up to ten colonies, with retention between 90% and 94%. The aerial disturbance caused by vacuum-cleaner exhausts was also investigated; slit-sampler counts following the discharge of exhaust inside a small room showed that with open jet exhausts there was an immediate rise and fall in the number of airborne bacteria, followed by a slow bacterial fallout over the next hour. When the speed of the airstream was reduced by means of a diffusing device at the outlet, no sign of disturbance was detected.

Vaginal Discharge

Dr. J. A. BOYCOTT (Taunton) said that of 561 specimens of vaginal discharge from women between the ages of 15 and 50, 418 contained little or no pus. The reaction, cytology, and flora of this non-purulent discharge made it probable that it was an exaggerated flow of the normal secretions of the vagina and cervix. 134 out of 143 purulent discharges contained trichomonas, with a mixed and inconstant bacterial flora. 9 purulent discharges appeared to be due to bacterial infection. Candida were found in 1 purulent and 64 non-purulent discharges. These yeasts might not be parasitic upon the vaginal epithelium but derive their nutrition from the secretions of the epithelium. In children below 15 and in women over 50 the picture was different. The discharge in 14 out of 16 children and 16 out of 18 older women seemed to be due to bacterial infection.

Aluminium and Pulmonary Fibrosis

Dr. G. B. MANNING (Bolton) described the case of a man aged 22 who died in 1954 from pulmonary fibrosis. 3 years 5 months before his death he had begun to work in an atmosphere heavily contaminated with aluminium powder. The next man who took over the identical job died of pulmonary fibrosis in 1959, 4 years 9 months after starting this work. A third case of fibrosis of lung from the same works was first suspected from the X-ray appearances of the chest before the place of work was known. This man had, in fact, spent only 1 year in that same factory.[1] Further investigations showed that so far out of 20 men exposed to heavy concentrations of aluminium powder in the atmosphere for more than 6 months, 2 had died from pulmonary fibrosis, 4 had evidence of pulmonary fibrosis, and 11 had normal chests; and 3 had refused examination.

Anæmia in Pregnancy

Dr. C. GILES (Stoke-on-Trent) reported a controlled trial of prophylactic folic acid during the last trimester of pregnancy, 758 women who received oral folic acid and iron showed significantly higher hæmoglobin levels at term than 721 women treated with iron alone. Megaloblastic anæmia developed in 20 cases of the control group but in none of the patients treated with folic acid. This trial supported the concept that folic-acid depletion tended to occur in late pregnancy, even in the absence of megaloblasts in the marrow. Analysis of 156 cases of megaloblastic pregnancy anæmia, diagnosed over a period of three years, suggested that an inadequate diet and intestinal malabsorption were important factors predisposing to megaloblastic anæmia. Abnormally high fæcal fat excretion was found in 12 out of 41 cases investigated, but in none of 17 normal pregnant women. When megaloblastic anæmias of pregnancy were classified according to the types and relative numbers of megaloblasts in the marrow. an abnormal blood-group distribution, with a significant increase of group A, was found in cases with the more advanced degrees of megaloblastosis. These findings suggested that folic-acid deficiency tended to occur in a large number of women in late pregnancy, but only in a certain group, with an inherited predisposition, would folic-acid depletion result in florid megaloblastic anæmia.

Bone-marrow Grafting in Man

Dr. J. G. HUMBLE (Westminster Hospital) said that in 6 out of 8 patients treated by whole-chest irradiation for malignant

1. *Brit. J. industr. Med.* 1959, **16**, 123.

disease marrow function was restored to the sternum by stored autologous marrow. In 4 out of 9 cases treated by massive chemotherapy marrow function was similarly restored.[1] The other patients died before marrow function could be restored. Some evidence of effect of the treatment on the tumours was noted. The danger of infection, especially moniliasis, was considerable. Despite recent criticism, the results suggested that a true reseeding of the marrow spaces took place. Using homologous transplants, 3 cases of aplastic anæmia and 5 of acute leukæmia had been treated. No remissions had been obtained although the last leukæmic child treated was showing hæmatological recovery when overwhelming moniliasis supervened. The use of stored autologous marrow gave a much greater margin of safety in the vigorous treatment of malignant disease.

Intestinal Biopsy in Cœliac Disease

Dr. A. H. CAMERON (Birmingham) described the histological findings in duodenal or jejunal biopsies from 37 children, of ages ranging from 3 months to 4 years. Using a technique for estimating the relative surface area of the mucosa, the biopsies were separated into two groups. The first showed no significant loss of mucosal surface area, and they came from 11 patients, 1 of whom had cœliac disease and had responded well to gluten-free diet: the other 10 showed no clinical evidence of cœliac disease. Of the remaining 26, the clinical diagnosis was cœliac disease in 21, probable cœliac disease in 4, and uncertain in 1. Only 1 was on gluten-free diet at the time of biopsy. This group was subdivided according to the severity of the histological appearances. The histological grading might be of value in evaluating response to therapy. Dr. Cameron concluded that biopsy was a safe and important method of investigation in steatorrhœa of childhood.

Coagulation Tests on Capillary Blood

Dr. KATHARINE DORMANDY and Dr. R. M. HARDISTY (Great Ormond Street) reported a scheme for the routine investigation of coagulation disorders using free-flowing capillary blood. 0·2 ml. blood was taken into a buffered citrate-saline mixture and used for the "prothrombin and proconvertin" test of Owren and Aas [2] and the thromboplastin screening test of Hicks and Pitney [3]; the clotting-time of the capillary blood [4] was also determined. These three tests were used as screening procedures; accurate identification of any defects revealed could be achieved by assay procedures carried out on the same specimen of blood. The sensitivity and accuracy of the tests were indicated by comparison with the results of tests performed on venous blood obtained simultaneously.

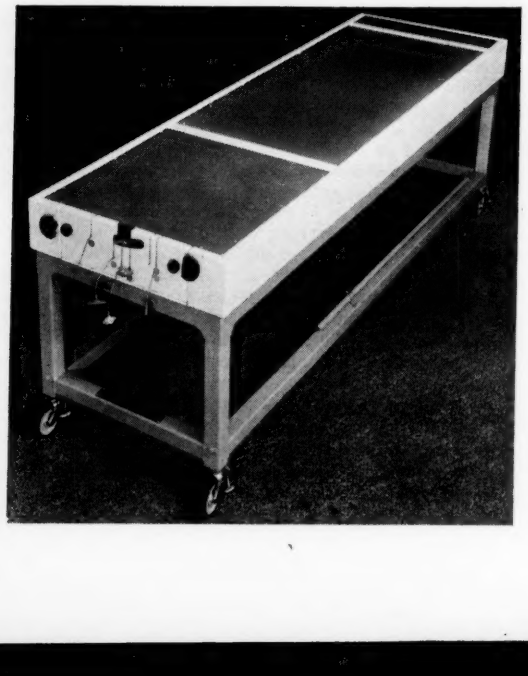
2. Owren, P. A., Aas, K. *Scand. J. clin. Lab. Invest.* 1951, **3**, 201.
3. Hicks, N. D., Pitney, W. R. *Brit. J. Hæmat.* 1957, **3**, 227.
4. Dale, H. H., Laidlaw, P. P. *J. Path. Bact.* 1911, **16**, 351.

New Inventions

A TABLE FOR SERIAL ARTERIOGRAPHY OF THE ABDOMINAL AORTA AND LEG VESSELS

VARIOUS methods of serial radiography of the arterial systems of the abdomen and legs, using a single dye-injection technique, are available. The special table here illustrated, which has proved satisfactory in the South Warwickshire group of hospitals, is a reproduction, with certain modifications in detail, of a table designed and pioneered by Prof. J. B. Kinmonth, in association with the radiographic departments of St. Thomas's and St. Bartholomew's Hospitals.

Three complete exposures of the abdomen and legs are obtained by using a series of sliding trays. A device is incorporated to overcome the inevitable gap between abdominal and leg films if a conventional technique is used. Casettes are employed for the abdominal pictures, and overlapping double-wrapped films for the upper and lower legs. Two X-ray tubes are required, the lower covering both leg films. This lower tube can be a standard hospital mobile X-ray Unit (60 mA) to which a special large rectangular cone must be fitted. The pictures are improved by incorporating a wedge filter in this unit. Alternatively the different exposures required for the upper and lower leg can be obtained by using double-wrapped films of different speeds. The table is loaded with films before the patient is placed there, and all further film changes are accomplished by one operator working at the head.



By using an elevating device, or simply wooden blocks at the upper end, the table may also be used for full-length leg phlebography.

I wish to thank Professor Kinmonth and Dr. J. W. McLaren of St. Thomas's Hospital for their assistance and kind permission to study their original plans; the staff of the X-ray department and the nurses at Warwick Hospital for their patient and willing help during the many clinical trials of the table; and the Cape Engineering Company of Warwick, who manufacture the table, for their interest, workmanship, and ability in overcoming the many technical difficulties encountered.

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Lakin Road, Warwick

C. R. SAVAGE
M.B. Lond., F.R.C.S.

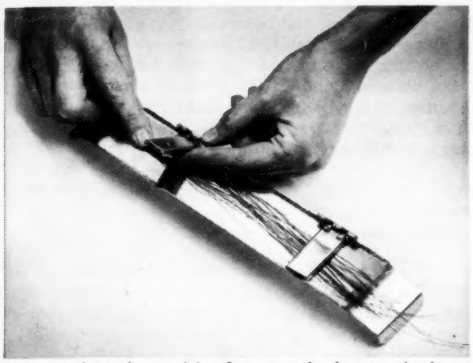
A DISPENSER FOR NYLON SUTURES

HOLDING suture material is not an important problem in general surgery, but for casualty work, where cheaper heat-sterilised nylon sutures are often used, immediate access to a supply of previously sterilised sutures is desirable.

A well-known means of dispensing sutures by threading them through a short rubber tube was used for a time in the casualty department of Leeds General Infirmary, but this proved inconvenient since the rubber deteriorated with use, and the sutures became untidy during boiling.

A dispenser was therefore designed by Mr. Maurice Ellis, consultant in charge of the department. This was non-corrodible, held about twenty 14-in. lengths of nylon firmly during sterilisation, and allowed any desired number of sutures to be removed easily when it was placed in a sterile instrument cupboard. The dispenser comprised three stainless-steel helical springs held parallel in a rigid frame, the overall length corresponding to the length of the sutures. Single strands of nylon could be pushed between the coils of the springs so that each was held firmly and could be withdrawn separately.

But this device required several minutes to fill, and occupied a relatively large area in proportion to the number of sutures held. I therefore designed a further device (see figure). Also made from stainless steel, it comprises a flanged base-plate 16 in. long and 1–2 in. wide with two flanged spring-loaded flaps, which hold an unsorted bundle of sutures. Because the



sutures are thus clamped by four metal edges, a single suture may be withdrawn leaving the remainder undisturbed. Each end of the base-plate slopes away for 1 in. to facilitate picking up the sutures with instrument forceps. This dispenser is easily and rapidly loaded, and is suitable for all gauges of nylon suture. It has been in use in the department for a year, and has proved reliable and convenient.

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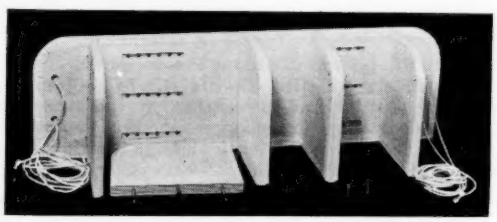
B.A. Oxon.
Casualty Dresser

University of Leeds,
Medical School, Leeds, 2

A FOOTBOARD TO KEEP THE FEET IN THE CORRECT POSITION

DEFORMITY of the feet is an end-result of many diseases. Fixed plantar flexion not uncommonly follows footdrop, whatever its cause. Sandbags are often the only means used to support the feet at right angle, but these rarely stay in place for long, and they tend to produce a claw-foot deformity.

The simple footboard illustrated here consists of a wooden board 2 ft. 6 in. long and 9 in. high, covered on its inner surface by thick orthopædic felt. The central partition is fixed to the board, and is covered on both surfaces with felt. The other four removable partitions are felt lined on their inner surfaces only. They are fixed to the board by upper and lower screws and wing nuts, and by a central peg, passing through any set of the three parallel rows of holes.



A foam-rubber pillow is placed under the patient's calves and the footboard is held firmly against the feet by cords which pass from the ends of the board and are tied at the bed head. Two small rear supports (not shown in the photograph) prevent the board from tilting backwards. The legs can be kept in adduction if placed between the central and inner removable partitions, or in abduction between the removable partitions. External or internal rotation deformities at the hip, which may follow paralysis of the legs, can be slowly corrected by gradually moving the partitions nearer together. If the knees are moderately flexed, a drawsheet, folded until it is 12–18 in. wide, placed across the knees and firmly tucked under the mattress is often helpful. A bed cradle is unnecessary when the footboard is in place.

The footboard was originally made for me eight years ago by the hospital carpenter. It is now manufactured by Messrs. Charles F. Thackray & Sons, of Leeds.

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ÆSTHESIOMETERS

THE æsthesiometers described here have been designed for testing two different aspects of touch sensation.

Threshold of Touch Feeling

The instrument shown in fig. 1 consists of an engineer's sliding calliper suitably modified. Two nylon threads of 0·02 in. (0·5 mm.) and 0·04 in. (1·0 mm.) diameter are passed through holes in the sliding part of the calliper and fixed by screws in the handle. In testing a patient the tip of one of the threads is brought gently into contact with the skin and the thread is then distorted through a distance of two or three millimetres, this distance being judged by taking the tip of the other thread as a reference point. The strength of the stimulus is directly related to the working length of the thread—that is, to the distance between the free end and the hole in the sliding part of the calliper. The weight of the thread can be ignored provided the instrument is held in the same position relative to the skin surface when two areas of skin are compared.

The threshold of touch feeling is greatly influenced by skin temperature, so absolute values cannot be conveniently obtained. Relative values, however, can be obtained by comparing an abnormal area of skin with a normal area. Sensory maps can be easily made by using a stimulus which is just subthreshold in an abnormal area since this stimulus will probably be well above the threshold in neighbouring normal areas.

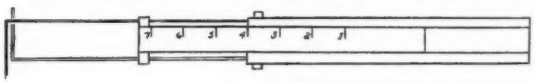

Fig. 1—Æsthesiometer for touch feeling threshold (half actual size).

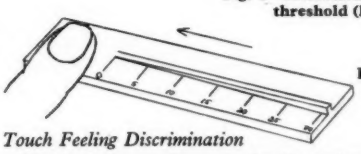

Fig. 2—Æsthesiometer for touch feeling discrimination (half actual size).

Touch Feeling Discrimination

The instrument shown in fig. 2 consists of a piece of transparent acrylic, 10 × 2 × 0·3 cm. in size. A ridge runs down the middle projecting 0·03 in. (0·75 mm.) at one end and gradually diminishing to zero about 2 cm. from the other end. The instrument is marked at points where the projection measures 5, 10, 15, 20, 25, and 30 thousandths of an inch, or in fractions of a millimetre if this is preferred. The markings are placed on the surface opposite to the ridge contrary to the appearance in the figure.

The flat end of the instrument is pressed on the patient's fingertip and then moved lengthwise across the finger until the patient announces that he can feel the ridge. This is done two or three times to allow the patient to improve his performance. The upper limit of normality is 0·01 in. (0·25 mm.) in all fingers except the fifth, in which the upper limit is 0·015 in. Most subjects can feel 0·005 in. on the index finger. The test should be carefully restricted to the part of the phalanx midway between the centre of the whorl and the fingertip, for proximally the threshold rises rapidly. Care has also to be taken to keep the ridge moving in the direction of its long axis; for a movement in any other direction causes the ridge to scrape the skin, producing something akin to a vibration feeling. This test is not influenced by skin temperatures.

This test can be substituted for tests of postural sense in the hands and for tests of two-point discrimination, graphæsthesia, and so on. It is a more sensitive test and is easier for the patient and the examiner.

Touch feeling discrimination and other relevant matters are discussed elsewhere.[1]

Both instruments can be made without difficulty on a $3^1/_2$ in. lathe with a milling attachment. Information on making the instruments can be obtained from me.

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1. Renfrew, S., Melville, I. D. *Brain* (in the press).

Reviews of Books

Reflections of a Medical Investigator

R. A. McCance, C.B.E., F.R.C.P., F.R.S., professor of experimental medicine, University of Cambridge. London: Pitman Medical Publishing Co. 1959. Pp. 63. 7s. 6d.

This book contains four lectures delivered recently in Holland, and the reader will be rewarded by an insight into the opinions of a distinguished medical investigator. The opening chapter deals with some of the problems of modern medicine in which the applications of high-powered technology have to some extent been counterbalanced by equal concentration on the psychological aspects of illness. The great complexity of the doctor's responsibility for the patient's soma as well as his psyche is discussed with sympathetic insight. In the succeeding lectures Professor McCance covers many topics which he has made his own. Success in prolonging life brings us to the issue of food-supply versus population growth. It is to this very theme that Professor McCance has devoted much of his working life. He has dealt with famine and undernutrition at one extreme, and at the other he reveals his interest in over-nutrition and obesity. He also discusses the unique and temporary physiological states of early infancy where poor temperature regulation is counterbalanced by tolerance of oxygen lack. The problems of water balance at this early period of life, before the kidney has developed its full adult physiological functions, make fascinating reading. The author is at his best when he is dealing with his own investigations. He is perhaps a little less critical when discussing such questions as the relationship of dietary fat to atheroma. It is tempting to accept the simple explanation that the level of blood-cholesterol is all-important, but to do so ignores a vast accumulation of knowledge implicating a great variety of other factors. This little book will repay the few hours required for its study by its stimulating thoughts which are not readily available elsewhere.

Respiratory Physiology and its Clinical Application

John H. Knowles, M.D., chief of the pulmonary disease unit and assistant in medicine, Massachusetts General Hospital, instructor in medicine, Harvard Medical School. Cambridge, Mass: Harvard University Press. London: Oxford University Press. 1959. Pp. 256. 42s.

The first part of this book describes different aspects of pulmonary function in health and disease, gives an account of tests in current use, and discusses the interpretation of findings. Emphasis is placed on tests which demand only those laboratory facilities likely to be available to the practising physician. The second part of the book describes the alterations in pulmonary function associated with individual disease processes. The story is told as far as possible in words; statements in symbols and equations are translated for the benefit of readers unfamiliar with the language of mathematics. The content of this work is first-class, the presentation succinct, and the style lucid. There is an excellent bibliography. The author has aimed at the interested clinician and it is safe to predict a palpable hit.

Christ and Freud

Arthur Guirdham, D.M., B.SC., D.P.M. London: Allen & Unwin. 1959. Pp. 193. 21s.

The author gives his personal views on the relationship between psychiatry and religion, comparing and strongly criticising doctrinaire aspects of both religion and psychoanalysis. The Church's preoccupation with sexual sin and guilt and the analytic overemphasis on the avoidance of frustration he views with disapproval, although religious experience, distinguished from "Religion", and many Freudian ideas are regarded with sympathy. On the practice of psychiatry he says much and attacks the tendency to become preoccupied with the patient's possibilities of self-expression, personality development, and social participation. He favours instead the negation of personality by techniques of contemplation, self-analysis, and relaxation, showing throughout the book that sympathy for Buddhist concepts which appears to be the contemporary trend. The book is interestingly written and not without humour, though it is marred by trenchant criticism of ideas no longer held and a few doubtful assertions —for example, that neuroses are of infinitely smaller incidence against a Buddhist or Hindu background.

Laboratory Manual of Pediatric Micro-Biochemical Technics

Editors: Donough O'Brien, M.D., M.R.C.P.; Frank Ibbott, F.I.M.L.T., department of pediatrics, University of Colorado. Colorado: University Medical Press. London: H. K. Lewis. 1959. Pp. 164. 21s.

This spiral-backed manual, printed in typescript form, has been prepared at Colorado University by the two authors, who had previously been associated with The Hospital for Sick Children, Great Ormond Street. The manual is intended for residents in clinical pathology passing through the chemical pathology departments in the course of their more general training, and also for trainee technicians and other clinical chemists who have need of techniques specially adapted for children. Methods are alphabetically arranged, rather as they would be in a laboratory notebook, providing a useful form of ready reference.

Yours by Choice

A Guide for Adoptive Parents. Jane Rowe. London: Mills & Boon. 1959. Pp. 148. 15s.

The title rather suggests that those who would like to choose a child for themselves can do so, and the subtitle that the contents will tell them how to set about it. Actually the reader will learn that choice is severely limited and that many who think of adopting should search their hearts and refrain. The rather complex legal machinery, varying from country to country even within these islands, is only lightly sketched; there is no index, and as a guide it must be called incomplete. As a book of advice, especially on the many emotional problems inherent in adoption and arising from it, on the influences of inheritance and environment, and on the credits and debits of the undertaking, it is well informed, well balanced, and a useful addition to the growing literature of the subject. Adopters, prospective or actual, will find it interesting and thought-provoking and are almost certain to get help from its pages; but they should regard it as a commentary rather than a guide.

Oxygen Supply to the Human Fœtus (Oxford: Blackwell Scientific Publications. 1959. Pp. 313. 47s. 6d.).—There were twenty-one distinguished participants in this symposium organised jointly by the Council for International Organisations of Medical Sciences and the Josiah Macy, Jr., Foundation, and held in December, 1957. This book is a well-produced record of their deliberations, ably edited by Prof. James Walker and Dr. A. C. Turnbull. It is not a verbatim report and there is possibly some loss in spontaneity and speculation, although revision and rearrangement have made it coherent and readable. Three main areas are fully explored: the physiology of oxygen transport in fœtal blood, a subject about which much is known, although the practical importance is undetermined; the uteroplacental circulation, a problem of immense significance about which almost nothing is known, though the contributions of Ramsey, Metcalfe, and Browne are all exciting pioneer ventures; and, thirdly, the measurement of cord-blood oxygen levels, a controversial subject which is fully discussed with differences and difficulties frankly reported. Throughout runs the troubling thought that, however meticulously sampled and analysed, the cord-blood at birth may not be wholly representative of "the oxygen supply of the human fœtus". Anyone interested in the fœtus and infant would profit by reading this very useful book: for one thing readers will be led away from the pitfall of too facile a translation of experimental results to clinical practice, and they will appreciate the slow and painful way in which fundamental knowledge in this area is being acquired.

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Renal Hypertension

THE growing recognition that unilateral renal disease of many different kinds can cause high blood-pressure confronts the clinician with a particularly difficult dilemma. For on the one hand it encourages him to hope that he may meet the occasional case of hypertension which will respond dramatically to surgery, while on the other it faces him with problems of diagnosis and treatment which seem to grow daily in complexity.

In the first place curable renal hypertension is much less common than, and at the same time clinically indistinguishable from, essential hypertension. Secondly, some of the methods used in its detection, such as aortography, are technically difficult, by no means free from danger,[1] and not always reliable. The first problem, then, is to choose which patients should be submitted to special investigation, and a considerable number of pointers have been suggested [2–4] since PLATT [5] first pointed out that lack of a family history of hypertension may sometimes be significant. Thus PEART,[2] whose Goulstonian lectures for 1959 include a valuable analysis of the problem, mentions an abrupt transition from the benign to the malignant phase, polyuria and proteinuria, disparity in size of the kidneys, and, in the case of stenosis of a renal artery, loin pain, leucocytosis, and a murmur over the abdomen. Unilateral impairment of renal function is also suggestive. To these CONNOR et al.[3] would add the onset of hypertension at an unusually early or late age—that is, under 30 or over 50—and a history of abdominal injury. None of these pointers can ever be more than suggestive. The renal disease may be only apparently one-sided. If it is in fact unilateral it is not necessarily the cause of the hypertension. And if it is the cause it may have led to secondary hypertensive damage in the opposite kidney.[6] What is clearly needed is a reliable criterion for resolving these complexities. Some recent work by HOWARD et al.[3 7] at the Johns Hopkins Hospital goes at least part of the way towards providing such a criterion.

The work was prompted by the observation in animals [8 9] that in hypertension caused by constricting one renal artery the urine excreted by the "ischæmic" kidney is greatly reduced in volume and contains an abnormally low concentration of sodium. In a series of 210 hypertensive patients the Baltimore workers passed catheters up both ureters and compared the volume and sodium content of the urine from the two kidneys. In 18 of these patients a kidney was later removed in the belief that it was causing the hypertension. In 8 out of 9 patients whose hypertension was not relieved by nephrectomy the volume of the urine from the affected kidney was reduced, often considerably, but the sodium concentration was either equal to or *greater* than that of urine from the opposite kidney. On the other hand, in 9 patients relieved or cured by nephrectomy both the volume and the sodium concentration of urine from the affected kidney were reduced—the volume by at least 50% and the sodium concentration by 15% or more. These results suggest strongly that this test should be applied to all hypertensive patients before renal surgery is undertaken. But, as the Baltimore and other workers point out,[3 4] failure to demonstrate unilateral impairment of renal concentration of sodium does not necessarily imply that the kidney concerned is not causing hypertension. One situation where such a negative result may be misleading is where the underlying circulatory abnormality—whether it be pyelonephritis,[10] stenosis of a major artery, or any other lesion—may involve only a portion on one kidney, the rest of which may follow the excretory pattern of the opposite kidney.

The clinician's problems do not end with the decision that a kidney is probably at fault, for he has yet to decide on treatment. In some cases nephrectomy is the only choice; but in others, and especially in renal arterial stenosis, a wide range of more difficult operative measures have to be weighed against simple nephrectomy.[2 3] Many clinicians have been disappointed with the results of operation. But where thorough investigation and careful selection of patients have been possible, the proportion of favourable results has been around 50%.[3 4 11] This is very good in the circumstances; but it is still not good enough. It must be remembered that erroneous selection for operation will not only do no good: it may aggravate the hypertension, for in experimental hypertension removal of normal kidney tissue raises the blood-pressure considerably.[6]

All in all there can be few more difficult problems in practical medicine today; but great progress has been made, and to cure even the occasional patient of severe hypertension is no small achievement.

Only Isoniazid

IN severe pulmonary tuberculosis isoniazid alone gives results inferior to those obtained with streptomycin and isoniazid, streptomycin and *p*-aminosalicylic acid (P.A.S.), or isoniazid and P.A.S. The two regimens most suitable for large-scale use are isoniazid with P.A.S., and isoniazid alone. Both these drugs are given by mouth, so large numbers of patients can be treated with a relatively small nursing staff; but P.A.S. has the disadvantages of high cost, large bulk, and gastrointestinal upset. Isoniazid alone is, therefore, a more attractive treatment. The use of isoniazid alone should be neither advocated nor condemned from its effects on a single

1. *Lancet*, 1958, i, 1058.
2. Peart, W. S. *Brit. med. J.* 1959, ii, 1353.
3. Connor, T. B., Thomas, W. C., Haddock, L., Howard, J. E. *Ann. intern. Med.* 1960, **52**, 544.
4. Page, I. H., Dustan, H. P., Pontasse, E. F. *ibid.* 1959, **51**, 196.
5. Platt, R. *Quart. J. Med.* 1948, **17**, 83.
6. Wilson, C., Byrom, F. B. *ibid.* 1941, **10**, 65.
7. Howard, J. E., Berthrong, M., Gould, D. M., Yendt, E. R. *Bull. Johns Hopk. Hosp.* 1954, **94**, 51.
8. Mueller, B. B., Surtshin, A., Carlin, M. A., White, H. L. *Amer. J. Physiol.* 1951, **165**, 411.
9. Berliner, R. W., Davidson, D. G. *J. clin. Invest.* 1957, **36**, 1416.
10. Kincaid-Smith, P. *Lancet*, 1955, ii, 1263.
11. Yates-Bell, J. G. *Brit. med. J.* 1959, ii, 1371.

type of the disease: in the past such generalisations have impeded progress in the chemotherapy of tuberculosis. The three main questions to be investigated are: (1) the efficacy of isoniazid alone in treating patients with cavities and tubercle bacilli in the sputum; (2) the efficacy of isoniazid alone, once the sputum has been made negative by combined drug therapy; and (3) the efficacy of isoniazid alone in treating from the start patients with no cavities and a negative sputum (this group would include those whose only abnormality is a positive tuberculin skin test). Even these divisions may be too general. Results obtained in hospital or by a well-staffed and efficient clinic might differ considerably from those in less favourable circumstances. Moreover, in certain circumstances the results in a particular class of patients might be much superior with P.A.S. and isoniazid together, whereas in other circumstances the difference might be less because more of those in the isoniazid group took the drug as prescribed than did those in the isoniazid-P.A.S. group. It is, of course, impossible to carry out controlled trials in all the possible combinations of circumstances that are found in practice throughout the world, and some extrapolation is necessary; but this must be applied cautiously.

The Medical Research Council's Tuberculosis Research Unit has carried out an impressive series of controlled field studies in the past fourteen years, each trial having been designed to answer one or more specific questions. In a joint trial [1] the results of twelve months' treatment of East African patients in hospital with isoniazid in high and low dosage, and with a low dosage of isoniazid given with P.A.S., have been compared.

The patients all had acute bilateral pulmonary tuberculosis with tubercle bacilli in the sputum, the cultures before treatment being sensitive to both drugs. One group (40 patients) received 100 mg. isoniazid twice daily. A second group (37 patients) received about 20 mg. isoniazid per kg. body-weight in two equal doses, those under 100 lb. (45·4 kg.) receiving 800 mg. daily, those above 100 lb. and below 120 lb. (54·3 kg.) 1000 mg., and those 120 lb. or more 1200 mg.; this high-dose group also received 200–300 mg. pyridoxine (about 5 mg. per kg. body-weight) each day. A third group (35 patients) received 100 mg. isoniazid and 5 g. of the sodium salt of P.A.S. twice daily in cachets containing both drugs together. Both clinically and radiographically the group treated with isoniazid and P.A.S. fared the best; the high-dose isoniazid group came next; and the low-dose isoniazid group did the least well. The bacteriological results are more important, for from these may be estimated the speed and extent of the decline of infectiousness in the groups and the emergence of resistant strains of bacilli. After three months' treatment 88% of the isoniazid/P.A.S. group had a negative smear, compared with 69% of the high-dose isoniazid group and 54% of the low-dose isoniazid group. After twelve months the culture results on single specimens were negative in 84% of the isoniazid/P.A.S. group and in 67% and 57% of the high-dose and low-dose isoniazid groups respectively. Because 5 in the low-dose and 6 in the high-dose isoniazid group had had chemotherapy changed because of deterioration, the twelve-month results give an unduly favourable picture. To allow for this and to give a more comprehensive assessment of the bacteriological status, the classification used by the Tuberculosis Chemotherapy Centre in Madras [2] was employed, the patients whose treatment was changed being classed as "bacteriologically active". By the stringent definition of all available cultures in the tenth, eleventh, and twelfth months being negative on culture, 58% of the isoniazid/P.A.S. group were "bacteriologically quiescent" after twelve months, compared with 34% and 25% in the two isoniazid groups. The proportions "active" were 19%, 54%, and 61% respectively. Sensitivity tests of cultures after six months' treatment showed isoniazid-resistant strains in 4 (13%) of the isoniazid/P.A.S. group, 16 (47%) of the high-dose isoniazid group, and 22 (61%) of the low-dose isoniazid group. The corresponding proportions at twelve months were 19%, 33%, and 53%. The catalase activity of these strains is unfortunately not stated.

This study shows clearly that in patients with severe infectious pulmonary tuberculosis treated in hospital isoniazid 100 mg. twice daily is much less effective than the same dosage of isoniazid with 5 g. sodium P.A.S. twice daily. Increasing the dose of isoniazid to about 20 mg. per kg. body-weight, given with 5 mg. pyridoxine per kg. body-weight, improves the results but does not bring them up to those obtained by combined treatment. There is some evidence that pyridoxine may interfere with the action of isoniazid,[3] [4] so in this trial the effective dose of isoniazid may have been less than the dose ingested. Better results might have been obtained without pyridoxine, but with more toxic effects on the central nervous system. Pyridoxine is expensive; at hospital prices in Great Britain isoniazid and pyridoxine in the doses used in the M.R.C. trial would cost from 2*s.* 6*d.* to 3*s.* 6*d.* a week for each patient, compared with 3*s.* for isoniazid with P.A.S. The weekly cost of 200 mg. isoniazid daily would be 2½*d.* per patient. But in mass treatment without adequate radiographic and bacteriological facilities, low doses of isoniazid alone seem unsuitable for infectious patients; and with high doses of isoniazid, although the bacteriological results are better, either pyridoxine must be added, bringing the cost to approximately that of isoniazid and P.A.S., or else a high incidence of peripheral neuritis must be accepted.

Little is known about the efficacy of isoniazid alone, once the sputum has become negative on culture. Possibly the bacterial population has by this time become small enough to be contained or killed by the continued isoniazid, the small isoniazid-resistant fraction being dealt with by the body's defences alone. But there seem to have been no satisfactory trials of such treatment, and without their support few clinicians would willingly change their practice of continuing two drugs for eighteen months to two years—though it may be unnecessary to continue the same doses of the drugs or to give them as frequently as in the early stages. Investigation of regimens for continued treatment

1. East African/British Medical Research Council Isoniazid Investigation. *Tubercle, Lond.* 1960, **41**, 83.

2. Tuberculosis Chemotherapy Centre. *Bull. Wld Hlth Org.* 1959, **21**, 51.
3. McCune, R., Deuschle, K., McDermott, W. *Amer. Rev. Tuberc.* 1957, **76**, 1100.
4. Boone, I. W., Strang, V. G., Rogers, B. S. *ibid.* p. 568.

would be difficult, but the results might lead to considerable saving of money and enable better initial treatment to be given to larger numbers.

Isoniazid has been used extensively for treating people whose only evidence of tuberculosis is a positive tuberculin skin test.[5 6] Unfortunately, there is no information yet about the risk of isoniazid-resistant strains of tubercle bacilli emerging if the patient becomes infectious later. It seems to be agreed that this risk is probably very small; but in planning mass treatment of non-infectious patients, even an approximate estimate of its extent would be helpful. Too little is known also about the long-term effects of any type of chemotherapy of patients with radiographically manifest lesions but no evidence of infectiousness or progression. The Tuberculosis Society of Scotland [7] carried out a controlled study, using isoniazid and P.A.S., in patients with pulmonary lesions of "doubtful" activity and over a period of two years found fewer relapses in the treated group. In a study by HALL et al.[8] of 27 patients in whom there had been no radiographic change for at least three years and who had not previously received chemotherapy, there was no deterioration during a year's prescribed treatment; of 28 who were observed but not treated 1 deteriorated. The patients received isoniazid with calcium benzoyl P.A.S., and as this substance gives such low concentrations of P.A.S. in the serum [9] the effect of the combination might be regarded as almost the same as that of isoniazid alone. PHILLIPS [10] reported that in patients with slight or moderately advanced disease without cavities the results with isoniazid alone were probably equally as good as those with isoniazid and P.A.S. The M.R.C. East African study has provided a little further information. There were 25 patients with no or only slight cavitation: at twelve months the numbers with single sputum specimens negative on culture were 8 out of 10 in the isoniazid/P.A.S. group, 3 out of 3 in the high-dose isoniazid group, and 7 out of 11 in the low-dose isoniazid group.

Isioniazid alone is now being advocated as part of the programme to eliminate tuberculosis in the U.S.A. A conference arranged by the U.S. Public Health Service and the National Tuberculosis Association has recommended [11] that chemotherapy be applied primarily as a "public health tuberculosis control measure", and that all resources be mobilised "for a widespread application of the scientifically demonstrated and medically accepted procedures of adequate chemotherapy". The conference did not specify the forms of chemotherapy. OATWAY [12] had previously suggested giving isoniazid alone for at least a year to those believed to have "inactive" tuberculosis; and ISRAEL [13] advocates a vigorous campaign to treat with isoniazid those with "inactive" lesions or with lesions "of doubtful clinical significance". MCDERMOTT,[14] however, commenting on the recommendations of the conference, suggests that the safety of extending the use of isoniazid alone beyond those with positive tuberculin reactions but without obvious disease is "a matter of serious debate". ISRAEL contends that such extension would bring the anti-tuberculosis campaign in the U.S.A. to a dramatic end, and that, if a campaign of elimination has to be deferred for many years until evidence of the effectiveness of isoniazid alone is obtained, "anti-tuberculosis programs will fizzle out and the opportunity for a telling blow will have been lost". The arguments for an isoniazed attack on tuberculosis throughout the world command respect; but it is doubtful whether such an immense enterprise should be initiated without some valid evidence that the cost and trouble are worth while.

5. International Tuberculosis Conference. *Bull. Un. int. Tuberc.* 1959, **29**, 152.
6. Lambert, H. P. *Amer. Rev. resp. Dis.* 1959, **80**, 648.
7. Tuberculosis Society of Scotland. *Tubercle, Lond.* 1958, **39**, 129.
8. Hall, Z. M., Zorab, P. A., Jefferson, K. E. *ibid.* 1960, **41**, 47.
9. Leading article. *ibid.* 1959, **40**, 133.
10. Phillips, S. *Amer. Rev. resp. Dis.* 1959, **80**, 641.
11. Recommendations of the Arden House Conference on Tuberculosis. *ibid*, 1960, **81**, 482.
12. Oatway, W. H. *ibid.* 1959, **80**, 108.
13. Israel, H. L. *ibid.* 1960, **81**, 581.

Annotations

PSYCHIATRY AND THE MEDICAL STUDENTS

IT is often (and rightly) said that British medical schools pay too little attention to the undergraduate teaching of psychiatry; but few who heard Prof. John Romano on April 27 can before have realised just how great the gulf is between curricula on either side of the Atlantic. Speaking at the London Hospital Medical College, Dr. Romano placed a heavy task on teachers of psychiatry—essentially this was the "scientific humanisation of biology". They must teach the sequence of events in human growth and decline, and the relations between the patient and others, especially the physician, and in turn the physician's relations with ancillary staff. The student needs to learn the history of the concepts of health and disease leading to the current multiple-cause "open" system, and how to listen to and record the patient's story. He must become aware of changes in medicine and in society, and be sensitive in perceiving certain types of criminal and social behaviour as variants of health and sickness. He needs to grasp the uniqueness of the individual human being and appreciate the normal emotional crises of family life; but above all the teacher must foster the critical pursuit of knowledge and prepare the student to handle patients who manifest pain, anger, fear, anxiety, shame, and guilt in various psychological and somatic ways. It was essential, continued Dr. Romano, that we put behind us the vague dichotomy of "scientific" bodily disorder versus "intuitive" psychiatry; a logical approach to the mind is increasingly possible and the useful collaboration of psychoanalytic institutes with medical teaching in the U.S.A. helps in presenting the student with a framework of hypotheses. The Americans, one might add, have an advantage over us in this, for most of our teachers of psychiatry are so incapable of making up their minds on Freud that they ignore his massive contribution. Despite the distressing susceptibility of American psychiatry to psychotherapeutic and pharmacological fads, Dr. Romano thinks that it holds a satisfactory position between Russian environmentalism and European determinism. High standards of life, ease of communication, and freedom from catastrophic disease had allowed the discipline to advance more readily, perhaps, than elsewhere. The vigour of American psychiatry was

14. McDermott, W. *ibid.* p. 579.

certainly suggested by the extensive undergraduate preparation which tried to accomplish the triple aims of training appropriate to future psychiatrists, family doctors, and other specialists.

Subjects covered in the two preclinical years at Rochester, New York, are personality growth, psychopathology, interviewing, and the patient-physician relationship. 70 students attend two-hour weekly sessions over the first year of thirty-six weeks, for a lecture followed by discussion in small groups, each under a senior staff member. In the second year the students spend two $1^1/_2$-hour sessions per week and there is attendance at nurseries and a course in history-taking. Films, tape-recordings, and one-way screens (with the patient's knowledge) are freely used and the course is compulsory. It is rightly held that such study is basic and fundamental to the whole of medicine. In the third year, students work in the 775-bed hospital in which 86 beds are devoted to adult and 12 to child psychiatry, and in the outpatient department, where 12,000 patient-visits were made in 1959. 6 to 8 students at a time spend four weeks full-time serving 2–3 inpatients each per week. There are no clinical lectures, but seminars are held and the very large psychiatric staff (18 full-time, 34 part-time plus 24 residents and research fellows and 6 interns) allow for continual individual teaching and supervision. The fourth-year course is much the same, with outpatient responsibility and supervised individual psychotherapy with patients and their families. Liaison with medical and pædiatric departments is close, and visits are made to the Rochester State Mental Hospital (3500 beds) and to institutions for epileptics, delinquents, and defectives. Students with aptitude and interest may extend their course and undertake research, or join colleagues from other universities for special elective work during the summer. The teaching process itself is constantly under examination and review by students and teachers alike. The fuller approach may be easier for American students who, at 21–22, come to their studies at a maturer stage, but the course is emphatically pedagogic rather than therapeutic. Although, as Dr. Romano admits, American developments in this field are rather uneven, he hopes that his faculty is developing that systematic approach to man's mind, his emotions and relationships with others which, with help from the physical sciences, must lead to a basic science of human behaviour.

Compared with the somewhat puny British efforts, this exhaustive training has an almost unreal grandeur and is unlikely to have other than a paralysing effect on deans of medical schools. In their recent valuable survey of psychiatric teaching here, the British Medical Students' Association have recorded an average of thirty-one hours' total lecturing over 17 medical schools, with about 3 ward-rounds and 8 outpatient sessions, nor is it likely that those schools failing to reply were any better.[1] Provision was alarmingly disparate, and the students showed themselves to be well in advance of their mentors in demanding more teaching, particularly in clinical work and psychotherapy.

A NURSE'S WORK

IN the U.S.S.R. psychoneurosis is one of the diseases for which nurses may receive industrial injury compensation; in Uruguay nurses receive a pension equal to their full salary at the age of 60; the United Kingdom is one of the countries in which the hourly rate of pay of a hospital staff nurse is lower than that of an unskilled labourer —there are three thought-provoking findings in the International Labour Office's study of the nursing profession.[2] Administrators, matrons, doctors, and members of hospitals boards and committees will find it informative and stimulating reading.

With the expansion of health and welfare services more and more nurses are working in clinics, factories, and the patients' homes; but the majority are still hospital-bound, and the conditions of work in hospital are inevitably criteria for the whole profession. The chief reason for the continuing wastage of nurses is marriage; yet, as the report points out, the arrangement of working hours in hospitals is not consistent with family life. Hospitals are trying to maintain a continuous service throughout the twenty-four hours of the day and the seven days of the week. Greater flexibility in the organisation of hospital work, it is suggested, would help to attract married nurses. One possible modification of the traditional pattern of hospital care is Monday-to-Friday wards.[3] Another possibility, as so many girls are marrying in their teens, would be to recruit more male nurses. At present the percentage of men in the profession varies: Austria has 1%, Barbados 0%, the United Kingdom 5%, Trinidad and Tobago 22%.

A chapter on health protection draws attention to the risks, old and new, to which nurses are exposed in their work. Shift work, which switches periods for sleep and work, makes special demands on nurses' health, and this is apt to be overlooked by hospital administrators who work regular "office hours". In most countries night duty is longer than day duty; but in Israel night duty is restricted to thirty-six hours a week while the day-duty week is forty-seven. The I.L.O. experts recommend "that occupational diseases and injuries connected with nursing work should be studied on a continuing basis and redefined at periodic intervals for purposes of entitlement to social security benefit." Nurses who have had to change their profession because of a violent allergy to one of the new pharmaceutical products, and others who have contracted an infection from a penicillin-resistant staphylococcus, will hope that this will lead to speedy official recognition of contemporary nursing risks.

RECURRENT RHEUMATIC FEVER

INHERENT in every attack of rheumatic fever is the threat of another. How reliably does the pattern of a first attack enable the severity of a recurrence to be predicted? The answer to this question, always important to an anxious parent, has assumed greater significance since the introduction of effective means of reducing the risk of recurrent attacks.[4] After observing a large number of children and young adolescents who had had at least two attacks, Feinstein and Spagnuolo[5] have found that recurrences run very true to the form of the first attack, particularly as regards cardiac features.

Their investigation at first embraced 24 patients who had been examined in one institution and to whom uniform criteria for the diagnosis both of rheumatic fever[6–8] and of valvular disease had been applied. In this group both initial and subsequent attacks were personally observed by the authors. To these cases were later added 137 more, personally examined under the same uniform conditions only in recurrent attacks; data concerning the first attack in this second group were derived from the records of other physicians.

The results of this investigation were strikingly clear-

1. Report on the Teaching of Psychiatry and Psychological Medicine in British Medical Schools. British Medical Students' Association. (Undated, I am pretty sure 1960).
2. Employment and Conditions of Work of Nurses. Geneva: International Labour Office. 1960. Pp. 176. 12*s*.
3. Simpson, M. *Lancet*, April 30, 1960, p. 977.
4. See *ibid*. p. 967.
5. Feinstein, A. R., Spagnuolo, M. *New Engl. J. Med.* 1960, **262**, 533.
6. Jones, T. D. *J. Amer. med. Ass.* 1944, **126**, 481.
7. American Heart Association. *Mod. Conc. cardiov. Dis.* 1955, **24**, 291.
8. Feinstein, A. R., Di Massa, R. *New Engl. J. Med.* 1959, **260**, 1001.

cut. With very few exceptions patients who had no organic murmur during one attack emerged equally unscathed from the next. If an organic murmur had been audible during the earlier illness cardiac damage persisted, recurred, or increased during subsequent episodes. 61 patients escaped damage to valves in 129 attacks of rheumatic fever, and in 90 such damage was evident in each of their 211 attacks. This left only 10 cases in which organic murmurs were recorded for the first time during a recurrence; all were cases in which information about preceding attacks was extracted from the records of other physicians, and in 8 the negative auscultatory findings in these past episodes were regarded as questionable. Most of the patients were between 6 and 11 years of age, and within these limits cardiac damage had no predilection for any age-group. As Feinstein and Spagnuolo point out, this observation in a restricted age range does not invalidate the accepted concept that older patients with a first attack of rheumatic fever are less liable to cardiac complications. In patients who escaped damage to their hearts the pattern of non-cardiac manifestations—arthropathy, chorea, abdominal pain, erythema marginatum—in one attack tended to repeat itself in later attacks, but this tendency was less distinct when heart lesions were present.

Of the 121 recurrent attacks in 90 patients who had organic murmurs during the first attack, the original murmur persisted in 81, recurred in 34, and was replaced by a different murmur in 6. In 54 of these recurrences fresh cardiac damage became manifest through the appearance of new murmurs, further enlargement of the heart, congestive failure, or pericarditis. Hence the menace of recurrences was abundantly evident in patients who had had a previous attack during which an organic murmur had been heard. On the other hand, the older concept that recurrences are dangerous to *all* patients, including those whose hearts escape damage in the first attack, was not upheld. Feinstein and Spagnuolo ascribe this divergence from the traditional idea to their strict criteria for significant heart damage—criteria from which earlier work [5] had led them to exclude prolongation of the P-R or Q-T intervals in electrocardiograms and slight enlargement of the heart. As evidence of organic damage to valves they demanded a diastolic murmur audible at the base or left sternal border, or a systolic murmur (with or without a diastolic murmur in the same area) loudest at the apex and transmitted to the axilla. In their view it is only because organic murmurs are sometimes missed in first attacks that such murmurs are ever taken to be a new development in a recurrence. Aortic diastolic murmurs are particularly liable to be missed in this way.

In all, just over 60% of the patients in this series developed organic rheumatic valve disease—a figure similar to that reported from Boston by Bland,[9] who compared the severity of cases of rheumatic fever presenting at different times in the period 1921–51. While the incidence of organic valvular disease remained fairly stable (58–75%), the proportion of cases with severe cardiac enlargement fell during these thirty years from 30% to 14% and the five-year mortality-rate declined even more strikingly from 24% to 3%. Coupled with a decrease in incidence this decline in severity has reduced the stature of rheumatic fever as a cause of dangerous illness in children and of chronic cardiac invalidism. But as long as group-A streptococci survive in our environment and the pathogenetic link between the organism in the respiratory tract and the damaged valve remains obscure, there can be no certainty that rheumatic fever and rheumatic carditis will continue to dwindle in importance.

9. Bland, E. F. *ibid.* 1960, **262**, 597.

TRAINING IN RADIOLOGICAL HEALTH AND SAFETY

THE no. 1 pile at Windscale plutonium factory went wrong on Oct. 10, 1957; and the investigation of this accident first drew public attention to the national shortage of trained radiological health and safety specialists. This shortage was one of the main points emphasised in the report [1] of the Fleck Committee on the organisation for control of health and safety in the United Kingdom Atomic Energy Authority; and the report recommended that the Authority should take the lead in building up the national supply of health and safety specialists. A committee, under the chairmanship of Sir Douglas Veale, formerly Registrar of the University of Oxford, was accordingly set up to consider the need for specialists to deal with the health and safety aspects of the use of ionising radiations and radioactive substances. The report now published [2] makes recommendations about the types of experts needed and their training, and is at present being studied by the U.K. Atomic Energy Authority and the Government departments concerned.

The report describes the types of work involved in achieving radiological health and safety, and the kinds of training needed. It reviews the present position in this country and discusses the responsibilities of Government departments, local and public authorities, hospitals, and the medical profession, and nationalised and private industry. An estimate is attempted of the total number of trained people required during the next ten years. At the top level, university postgraduate courses have already been established to give a wide training—overlapping the boundaries of medicine, biology, physics, and chemistry—to selected graduates in science or medicine. There are courses at London and Birmingham, and the University of Edinburgh plan to start a course in October. The committee believe that these courses, fully developed, will meet the need for twenty or thirty top-grade specialists a year. The report recommends that similar courses of a less advanced kind should be set up at two or three colleges of advanced technology. At a lower level again, a scheme is suggested for introducing certificate courses at technical colleges in the autumn of 1961. Concerning the proposal for a national training centre, the committee consider it unnecessary, and recommend that the existing educational system should be used to provide the sort of training needed.

To make the best use of specialists, the report suggests a national radiological advisory service, with regional centres, to be set up under the Minister for Science. This service would advise organisations (such as firms making use of radioisotopes) without full-time health and safety specialists of their own. It would give expert help in the case of an accident involving possible radioactivity hazards.

The report also urges that all medical students should be given some knowledge of radiological health and safety in their undergraduate training, and that a course should be included in the curriculum for the diploma in public health.

1. Cmnd. 342. H.M. Stationery Office, 1958. See *Lancet*, 1958, i, 157.
2. Training in Radiological Health and Safety: Report of a Committee appointed by the United Kingdom Atomic Energy Authority. H.M. Stationery Office. Pp. 95. 5*s*. 6*d*.

Special Articles

OBSERVATIONS ON EXPERIMENTAL ANHIDROSIS

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Bannister's (1959) report that 12 soldiers developed total anhidrosis in the absence of miliarial lesions and pyrexia is of profound significance in relation to the pathophysiology of heatstroke. If case-histories can be trusted, many patients experience significant depression of sweating before the onset of hyperpyrexia (Hearne 1919, 1932, Ferris et al. 1938, Austin and Berry 1956). Not infrequently this depression begins a day or two before the heatstroke. One might expect, therefore, to find cases of anhidrosis which had not yet developed hyperpyrexia. Bannister's observations confirm this prediction. We should like to support his observations with an account of anhidrosis induced in volunteers participating in studies on survival rations. Some of this information has been given to the Central Society for Clinical Investigation (Sargent et al. 1956), but the only full report is in Air Force Technical Reports (Sargent et al. 1954, 1957).

At this point a word should be said on how anhidrosis or hypohidrosis was diagnosed among our subjects. At a time when the observer was sweating profusely, the skin of the anhidrotic subject was hot and dry to palpation both over the trunk and extremities and also in the axillæ and groin. The hypohidrotic subject had wide areas of hot dry skin but in other areas sweating could be detected by close inspection or palpation. Although Bannister (1959) does not give his grounds for diagnosis, the implication is that he, too, used clinical examination.

Observations

Experiences of 1953

Between January and June, 1953, a nutritional physiological investigation was made on eight students (Sargent et al. 1954). During a late spring heat-wave one of two men who were on a regimen of restricted water intake developed total anhidrosis.

SUBJECT 8 T, white male, aged 22, began eating a ration which provided 2000 kg. cal. per day (15% protein, 52% carbohydrate, and 33% fat) on May 25. He was allowed only 900 ml. water daily. On day 3 he complained of thirst, nausea, and depression. On day 4 he was still thirsty; 250 ml. of water was added to the allowance. On day 5 there was aching in legs, pallor, weakness, fatigue, and orthostatic light-headness. On day 6 he reported feeling " lousy ", weak, and tired; the tongue was dry and coated; 600 ml. of water was added to the allowance. Late this day pain appeared in the loins and there was tenderness to palpation. Urine: specific gravity, 1·034; no albumin; thick mucus; 2–4 leucocytes per low-power field; occasional finely and coarsely granular casts. On day 7 he was nauseated, dizzy, weak, tired, depressed, anorectic, and complained of pain in the loins. The oral temperature was not raised. There was total anhidrosis, but no evidence of miliaria; 195 ml. of urine was passed in 500 minutes (0·39 ml. per min.). Urine was as on day 6. A water-tolerance test was given. (Subject drank water load of 20 ml. per kg. bodyweight and urine was collected for 4 hours.) Within the 1st hour he felt dizzy and then exhibited an outburst of profuse sweating. 29% of the oral load was recovered in 4 hours. 4 hours after the start of the water-tolerance test, pitting œdema (+) appeared on lower extremities; next day it had disappeared. Unrestricted water was allowed and recovery was uneventful.

Daily maximum and minimum temperatures (°F) for May 25–31 were 88/67, 89/75, 75/47, 76/52, 90/54, 92/68, 92/69. This heat-wave provoked sweating in all our subjects. Two were on restricted water at this time and both were given extra water to compensate for the sweat-loss. Both complained of severe thirst and one (8 T) developed acute anhidrosis. While our data suggested that 8 T was dehydrated, he was no more dehydrated than the other subject on restricted water who did not develop anhidrosis.

Experiences of 1955

During the months of June and July, 1955, one hundred volunteer airmen were studied in a nutritional physiological investigation at Camp Atterbury, Indiana (Sargent et al. 1957). Forty-four of them had restricted allowances of water for 9 days, and in the first 7 days (July 6–12) there were three cases of total anhidrosis and eight of hypohidrosis among them.

TABLE I—ONSET OF ANHIDROSIS AND HYPOHIDROSIS IN RELATION TO TEMPERATURE AND HUMIDITY

Date of onset	Maximum temp. (°F)	4.30 P.M. relative humidity (%)	Number of cases	
			Anhidrosis	Hypohidrosis
July 6 ..	95	46	0	0
" 7 ..	92	54	0	0
" 8 ..	93	81	2	1
" 9 ..	99	81	1	1
" 10 ..	96	53	0	4
" 11 ..	94	35	0	1
" 12 ..	93	34	0	1
" 13 ..	95	34	0	0
" 14 ..	90	99	0	0

Table I shows that the temperature exceeded 90°F every day, and that on July 8 and 9 the relative humidity was 81%.

At first each man was allowed only 910 ml. water daily (one canteen). Because of the two cases of anhidrosis and the rapid weight-loss among these men, the allowances were increased on July 8 by one canteen to 1820 ml. for twenty-two men marching three miles a day and by two canteens to 2720 ml. for twenty-two men marching twelve miles a day. The hypohidrosis in some of the men marching three miles a day led to an increase of their allowance to 2720 ml. on July 11.

SUBJECT 74 H, white male, aged 18, had carbohydrate only (2000 kg. cal. daily). Each day he walked no more than three miles. On July 8 he complained of weakness, dizziness, occipital headache, and low back pain. (The last two symptoms had been persistent since he arrived at Camp Atterbury and were attributable to anxiety. They cleared rapidly in the recovery period.) Examination revealed a rectal temperature of 99·8°F, hot skin, total anhidrosis (including groin and axillæ), and slightly injected left eardrum. He had mild fever, an elevated pulse-rate both lying and standing, marked reduction

TABLE II—RECORD OF FUNCTIONAL TESTS ON SUBJECT 74 H

Date	Blood-pressure (mm. Hg)		Pulse		Oral temp. (°F)	Minute urinary vol. (ml.)
	Lying	Standing	Lying	Standing		
June 27 ..	145/80	142/105	68	96	98·6	2·41
July 2 ..	132/88	110/84	64	100	98·9	0·83
" 8 ..	135/82	134/90	88	128	100·0	0·25
" 11 ..	114/64	128/76	62	84	98·0	0·80
" 15 ..	108/68	129/95	68	108	98·2	0·54
" 20 ..	106/58	126/100	68	94	98·0	1·82
" 25 ..	128/66	126/94	62	96	97·8	1·17

TABLE III—WATER-TOLERANCE TESTS ON SUBJECTS 74 H AND 76 H

Date	Subject 74 H		Subject 76 H	
	Water load (ml.)	Net recovery* (%)	Water load (ml.)	Net recovery* (%)
June 28 ..	1445	38·7	1120	78·4
July 5 ..	1375	20·9	1120	35·2
„ 8 ..	1320	0·0	1065	2·1
„ 10 ..	1345	71·6	1075	11·3
„ 21 ..	1410	94·7	1130	86·5

* Volume of urine passed in four hours from start of test expressed as % of water load after correction for basal urinary flow.

of minute urinary volume, and no impairment of vasomotor reflexes (table II). In a water-tolerance test (table III) he began to sweat 8 minutes after starting to drink. The net recovery of the water load was zero. At this time, in spite of limited water intake, there had been a fall in the serum osmolarity and hematocrit (table IV). The results of this test were remarkable. Subjects on this nutrient regimen with restricted water intake generally show a diuresis as though they were not dehydrated (Sargent et al. 1959).

He remained in sick-bay until the next day. His nutrient regimen was not altered. During the rest of the experimental period, even though permitted unlimited water, he drank less than 1800 ml. daily. Presumably his lack of thirst was due to the pure carbohydrate diet (Sargent et al. 1957). Some additional dehydration developed, for on July 11 the hæmatocrit had risen to 46·5%, the maximum value for this man. Nevertheless, sweating was normal thereafter.

SUBJECT 76 H, white male, aged 18, had a high-protein high-fat ration yielding 1000 kg. cal. Each day he too marched three miles. On July 8, he reported to sick-bay complaining of substernal tightness of 20 hours' duration. Examination revealed an oral temperature of 99·6°F, pulse-rate of 144, cervical and axillary lymphadenopathy, total anhidrosis, and pharyngitis. He was moderately febrile and had a tachycardia and a relative increase of systolic and diastolic blood-pressure; but his vasomotor reaction to standing was normal (table V). The minute urinary volume was not reduced from previous

TABLE IV—BIOCHEMICAL MEASUREMENTS ON SUBJECTS 74 H AND 76 H

Date	Serum osmolarity (mOsm per litre)		Hæmatocrit (%)	
	74 H	76 H	74 H	76 H
June 27 ..	291	286	45·3	44·4
July 2 ..	287	292	43·6	44·2
„ 8 ..	272	300	43·0	47·5
„ 11 ..	283	284	46·5	49·0
„ 15 ..	276	282	44·0	47·1
„ 20 ..	282	274	42·6	43·9
„ 25 ..	280	278	45·0	44·0

values of the pre-period (June 27 and July 2). This failure of the minute urinary volume to decrease with limitation of water was caused by the high osmotic content of his nutrient regimen (Sargent et al. 1959). The low minute urinary volume of subject 74 H at this same time was due to the lower osmotic content of the pure carbohydrate regimen.

In a water-tolerance test (table III) only 2·1% of the oral dose was excreted. Within a minute of drinking, sweating began. At the time of the test this subject showed hæmoconcentration —elevated serum osmolarity and hæmatocrit (table IV). This behaviour was quite usual for men on diets with high osmotic content and restricted water.

He remained in the sick-bay until July 10; his nutrient regimen was not changed. Sweating continued normally for the rest of the experimental period.

On July 10 he was given another water diuresis test; only 11·3% of the test dose was excreted (table III). After drinking this water, no definite outburst of sweating was detected. One interesting comment, however, was made by the observer: 79 minutes after the test began, the left leg was hot and dry while the right leg was cool and damp with perspiration. Evidence of hæmoconcentration (elevated hæmatocrit) was still present on July 11 (table IV).

SUBJECT 33 H, white male, aged 18, had a high-protein high-fat ration yielding 1000 kg. cal. He marched twelve miles a day. After 24 hours of this regimen he began to complain of nausea, severe thirst, headache, abdominal pain, precordial pain, weakness, and dizziness. 2 days later (July 9) he was brought to the sick-bay complaining of an inability to sweat. He stated that he had felt hot for 36 hours. On the day before admission he drank only 1820 ml. of water. (His allowance was 2730 ml.) On the day of admission he had consumed 1820 ml. of water up to 4.30 P.M. On July 9 he had sweated normally in the morning. While marching back to camp after lunch, his fellow subjects remarked that his back was dry, even though the hike was done under a hot sun. At this time there was sweat on his forehead. He staggered while marching. During this march a headache developed and nausea which had started after breakfast persisted. He continued to sweat from his forehead until about 4.00 P.M., when all sweating ceased and he became progressively weaker and more dizzy. He reported urinary frequency but no polyuria. He was an

TABLE V—RECORD OF FUNCTIONAL TESTS ON SUBJECT 76 H

Date	Blood-pressure (mm. Hg)		Pulse		Oral temp. (°F)	Minute urinary vol. (ml.)
	Lying	Standing	Lying	Standing		
June 27 ..	108/80	100/65	60	100	98·6	0·57
July 2 ..	104/60	108/66	58	112	98·8	0·65
„ 8 ..	130/90	120/80	112	140	100·0	0·62
„ 11 ..	118/44	93/75	64	100	97·6	0·77
„ 15 ..	104/55	96/86	56	84	97·2	0·42
„ 20 ..	118/70	104/93	54	82	98·6	2·33
„ 25 ..	106/70	105/76	68	94	98·6	0·62

anxious-looking, well-developed, well-nourished young man. A sticky sound accompanied his speech. The tongue was thickly coated with café-au-lait coloured material. The skin was hot and completely dry. The groin and axillæ were also dry. There were no lesions of any kind on the skin. The oral temperature was 101·6°F and respiratory rate was 28. The pulse-rate was 100. The lying blood-pressure was 138/80 mm. Hg. Immediately on standing, the blood-pressure was 100/0 and one minute later while standing the pressure was 105/70. There was hyperreflexia of tendon reflexes.

He was confined to bed and his nutrient regimen was not altered. During the evening he drank some water from his remaining allowance (910 ml.) and ate meat bar which caused more nausea and cramps. At 10.30 P.M. the oral temperature was 99·0°F and total anhidrosis was still present.

On July 10, he was given special functional tests. The oral temperature was 97·6°F, the lying blood-pressure and pulse-rate 120/64 and 46, and the standing blood-pressure and pulse-rate 110/78 and 64. The minute urinary volume was 0·5 ml. per hour. He was still anhidrotic.

The decision was made to have him march (quarter-mile laps at 3·75 m.p.h.) in the afternoon to see whether sweating could be induced. During the march he was accompanied by a medical officer. Sweating did develop, especially on the forehead. During the fifth and sixth laps he complained of increasing sense of warmth, pressure on his chest, and dizziness. At the end of the sixth lap he was removed from the march. The pulse-rate was 148 and the rectal temperature 100·5°F. The respiratory rate was 43. He complained of tingling in hands, arms, chest, and mouth. A strongly positive Chvostek sign was elicited. 13 minutes later the only sweat was on the forehead. 16 minutes after the end of march paræsthesias of mouth and fingertips continued. At 19 minutes the rectal temperature was 101·4°F and the pulse-rate 76. At 44 minutes they were unchanged. At 46 minutes the tingling had disappeared. At 56 minutes the rectal temperature was 101·0°F and the pulse-rate 54. At 71 minutes the rectal temperature was 100·8°F and the pulse-rate 64. The sweat-loss during the march was 850 ml. per hour.

He spent the remainder of the day in the sick-bay. On July 11 he was released. Normal sweating had been restored.

TABLE VI—CLINICAL OBSERVATIONS ON EIGHT CASES OF HYPOHIDROSIS

Subject no.	Date of onset	Nutrient regimen	Clinical observations
26 H	July 8	Starvation	White male complained of dizziness, headache, thirst, and *dry skin.*
68 H	„ 10	Starvation	Negro male complained of abdominal cramps, drowsiness, *cessation of sweating,* and impending death. Water-tolerance test did not provoke sweating. Dry skin continued until July 12, when he was removed from experimental regimen.
70 H	„ 12	Starvation	White male complained of abdominal pain and weakness on July 11 and 12. *Skin dry* and face flushed on July 12. He was removed from experimental regimen.
73 H	„ 9	0/100/0* 2000	White male complained of *reduction of sweating.* No outburst of sweating during water-tolerance test of July 10
75 H	„ 10	30/0/70* 1000	White male complained of *reduction of sweating.* Skin was dry before water-tolerance test. Water load provoked a sweat response.
78 H	„ 10	30/0/70* 2000	White male collapsed after marching from camp in afternoon. Examination revealed oral temp. of 99·8°F, *hot dry skin with minimal sweating on forehead,* stertorous breathing, and premature ventricular contractions (one per 10 beats). There was an outburst of sweating shortly after beginning to drink water dose.
79 H	„ 10	2/20/78* 1000	White male complained of *reduction of sweating.* Sweating began on forehead several minutes after beginning to drink water dose.
82 H	„ 11	2/20/78*	White male complained of arm and leg cramps. Skin was pale and *dry;* hyperreflexia of tendon jerks. Water dose of preceding night caused moderate outburst of sweating.

* Percentage of protein, carbohydrate, and fat over daily caloric intake in kgcal.

Of the other men who had been on restricted water allowances, eight developed hypohidrosis. They had many of the same prodromal complaints as the three who became anhidrotic (table VI). (Note particularly the record for subjects 68 H and 78 H.) In most cases the symptoms came on immediately after the sultry period of July 8 and 9 (table I).

One case of hypohidrosis (26 H) was seen among the men marching twelve miles a day on the day when water allowances were increased for men on restricted water. After water allowances for men doing hard work had been increased to 2730 ml. daily, no further cases appeared in this group. The remaining cases were in men still allowed only 1810 ml.—i.e., men marching three miles a day. On July 10, when four cases of hypohidrosis appeared within this group, each was given a water-tolerance test and the daily water allowance was augmented to 2730 ml. After this alteration only two mild cases of hypohidrosis were seen. The general appearance and attitudes of all the men improved considerably.

Discussion

In these two investigations, four men with total anhidrosis and eight men with hypohidrosis were observed. All had been on restricted water, and they showed depression of sweating at a time of heavy demand on the evaporative mechanisms. None had significant pyrexia, any evidence of miliaria, or clinical signs of heat exhaustion. Of the nine who were given a water-tolerance test, seven sweated freely within a few minutes of beginning to drink. No cases of depressed sweating were seen among men allowed unlimited amounts of water, and no new cases developed among men whose allowance was increased from 910 to 2730 ml. daily, even though the weather remained hot (table I).

Two questions arise: (1) why the marked depression of sweating, and (2) why the outburst of sweating?

Depression of Sweating

The sixteen cases of anhidrosis and eight cases of hypohidrosis reported by Bannister (1959) and ourselves have two characteristics which cast doubt on current concepts of depression of the rate of sweating. Since none of the subjects had miliarial lesions, mechanical occlusion of the sweat-ducts by miliaria rubra or profunda (Sargent and Slutsky 1957) can be excluded. The anhidrosis of heatstroke is not caused by miliaria (Shelley, Horvath, and Pillsbury 1950). Ladell (1957) has suggested that cessation of sweating in heatstroke is merely a physiological reaction to a raised body temperature; but this view appears untenable. Thus suppression of sweating usually precedes the onset of symptoms of heatstroke (Hearne 1919, 1932, Ferris et al. 1938, Austin and Berry 1956, Medical Research Council 1958). Our cases of anhidrosis and hypohidrosis, and those of Bannister (1959) were all apyrexial. Hence it seems that in both heatstroke and " acute anhidrotic heat exhaustion " the depression of sweating is not due to hyperpyrexia. " Exhaustion of the sweating mechanism " was proposed by Hearne (1919, 1932) as the basis of heatstroke, particularly since he was unable to promote sweating with large subcutaneous injections of pilocarpine. This attractive hypothesis, however, has not been critically investigated in the climatic chamber, and one can only speculate that " sweat gland fatigue " might be the process common to both these types of depression of sweating.

Some investigators (Ladell 1955) report that dehydration depresses sweating; others (Adolph et al. 1947) say that it does not. Our subjects, like Bannister's, were dehydrated. The men with depression of sweating, however, were no more dehydrated than paired controls who did not develop anhidrosis or evident hypohidrosis (Sargent et al. 1957). Since no cases of anhidrosis or hypohidrosis were seen in men who were not dehydrated, the facts suggest that dehydration predisposes to these clinical episodes though it does not cause them. Perhaps it is for this reason that the literature on dehydration and rate of sweating is conflicting. It seems that we simply have not yet defined the true cause for apyrexial anhidrosis and hypohidrosis. The idea of " sweat-gland fatigue " does not aid much here, for such depression of sweating can occur in the absence of dehydration (Gerking and Robinson 1946, Thaysen and Schwartz 1955).

Outburst of Sweating

Our experience differs from that of Bannister. Whereas our men sweated very soon after drinking, his did not. Why he should have not seen this phenomenon is not clear, for it has been observed many times both in the laboratory and in the field (Saito 1930, Lee and Mulder 1935, Adolph et al. 1947, Lemaire 1954) even among men who were sweating normally. Our impression is that dehydrated men are more apt to show the outburst. The mechanism is unknown. Kuno (1956) has suggested that it is the result of a gastro-hypothalamic reflex, but his arguments are not convincing. Perhaps the drinking-hyperhidrosis is a distinguishing feature of this apyrexial anhidrosis. Since the anhidrosis of heatstroke cannot be broken by pilocarpine (Hearne), we are dealing either with different pathophysiological processes or with a less easily reversible stage of a process common to both.

Conclusions

These sixteen cases of anhidrosis among men without pyrexia and without miliaria (twelve reported by Bannister, four by us) raise new problems concerning the physiology and pathophysiology of sweating. Unravelling them will increase our understanding of the pathogenesis of heatstroke.

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Conference

RESEARCH IN THE CARIBBEAN

THE fifth annual scientific conference organised by the Standing Advisory Committee for Medical Research in the British Caribbean was held at the University College of the West Indies, Jamaica, on April 2–4. The topic for the meeting was the application of the laboratory to problems of clinical medicine. Prof. A. C. FRAZER (Birmingham), Prof. E. T. C. SPOONER (London), and Prof. G. BRAS (U.C.W.I.) took the chair in turn.

Cardiovascular Disorders

Hospital studies and field surveys were reported from Jamaica, Trinidad, British Guiana, and St. Kitts by Dr. J. A. TULLOCH (U.C.W.I.), Dr. G. WATTLEY (Trinidad), Dr. H. HAMILTON (British Guiana), and Dr. K. L. STUART (U.C.W.I.). Hypertensive heart-disease was the commonest cardiac cause for hospital admission, followed by luetic and then rheumatic heart-disease. Acute rheumatic fever was common and in Trinidad affected the East Indian more than the Negro. Cor pulmonale was uncommon in both Trinidad and Jamaica but was seen more often in British Guiana. In British Guiana and Trinidad it occurred almost exclusively in the East Indian. This racial difference could not be satisfactorily explained. Myocardial infarction was uncommon in all the territories. This was of interest because aortic atheroma was as common in Jamaica as in the United States of America although coronary-artery atheroma was less severe in Jamaica than in America.

A chest X-ray survey of 3000 people in Barbados showed a 10·7% incidence of cardiovascular abnormality and a considerable proportion had a positive serological test for syphilis. Yaws has not been recognised in Barbados for many years. This emphasised the fact that symptomless cardiovascular syphilis may be more common than has been thought and poses an important public-health problem. There was an urgent need for a test, serological or otherwise, that would differentiate syphilis from yaws.

Hypertension was common and field surveys in Jamaica and St. Kitts by Dr. STUART showed that blood-pressures in St. Kitts were slightly higher than those reported by the Medical Research Council team in South Wales, whereas in Jamaica the figures were comparable with those from South Wales. Dr. Stuart also described an investigation into significant bacilluria in the general population. There was a considerably higher incidence of bacilluria in the hypertensive female and this increased with parity. The relationship of bacilluria to hypertension was discussed and the possibility that pyelonephritis was responsible for the greater incidence of hypertension in the elderly female was suggested. A post-mortem study of hypertensive patients did show that renal hypertension was responsible for 50% of the cases and that chronic pyelonephritis accounted for a third of the renal cases.

Diabetes Mellitus

Dr. TULLOCH said that the prevalence of diabetes in Jamaica was a little over 1% of the adult population, and the ætiology seemed to be very similar to that reported from temperate countries. A consideration of the J-type cases by Dr. D. MACINTOSH (U.C.W.I.) and Dr. TULLOCH indicated that this was not a distinct type but was a phase in the natural history of the badly treated type-II patient.

Dr. T. POON-KING (Trinidad) reported that a considerable proportion of his cases responded satisfactorily to chlorpropamide. The distribution of blood-groups in diabetic subjects was also reported from Trinidad. In both males and females there was a low incidence in group O. Males showed an excess of group B and females an excess of group A over the local population as a whole.

Malnutrition

Dr. J. C. WATERLOW and Dr. D. I. M. PICOU reported preliminary observations from isotope studies in protein malnutrition. The economy of protein was achieved not by a decreased rate of catabolism but by increased reutilisation. Although the extent of protein synthesis might be reduced through shortage of supplies, the capacity for synthesis seemed in most cases to be unimpaired. Magnesium deficiency in malnutrition parallelled potassium deficiency and supported the view that there was a primary loss of intracellular constituents (Dr. R. D. MONTGOMERY).

Further investigations into the megaloblastic anæmia in malnourished infants were reported by Dr. J. E. MACIVER and Dr. E. H. BACK (U.C.W.I.). They showed that the cause was a dietary deficiency of folic acid, and that vitamin B_{12} was not implicated. Dr. MacIver also reported on the nature of the severe anæmic episodes in sickle-cell disease and showed that these were of two types. In one folic-acid deficiency was the ætiological factor and in the other there was an acute aplastic state. He suggested a possible relationship of the aplastic state to preceding infection.

Non-addisonian vitamin-B_{12} deficiency in the adult was reported from Trinidad by Dr. G. HABIB. All the patients were Hindus and with one exception they were strict vegetarians eating no eggs, meat, fowl, or fish. Poverty and a vegetarian diet seemed to combine to produce this deficiency state.

Dr. C. G. MILLER (U.C.W.I.) had found hepatomegaly in about 95% of all apparently healthy children under the age of 12 years. It was not related to malnutrition but the possible role of infection was considered. The necropsy incidence of cirrhosis of the liver as noted at the University College Hospital of the West Indies was much the same as in America. A third of all cirrhosis resulted from veno-occlusive disease of the liver.

Neurological Disorders

Dr. MONTGOMERY discussed the possibility that the unusual spastic neuropathies seen in Jamaica were related to treponemal infection. The neuropathy might be a late manifestation of treponemal infection, venereal or otherwise, and it might be due to a strain acting as a poor antigenic stimulus but producing a typical meningovascular lesion in the nervous system. A second neurological disorder in Jamaica, spinal arachnoiditis, was reported by Prof. E. K. CRUICKSHANK and Dr. P. E. RODGERS (U.C.W.I.). The ætiology was largely unknown but it had been found that cases seen early in the disease responded well to cortisone.

In England Now

A Running Commentary by Peripatetic Correspondents

DIALOGUE OF TOMORROW

SIR, can you tell me the meaning of an obsolete word? I know medical history is a hobby of yours.

I'll try. What word?

Auscultation.

It meant listening.

Listening to what, Sir?

Sounds made by the human body . . . I thought you'd be puzzled. Doctors used to listen to their patients' bodies, and palpate them directly, too.

Directly? You mean they used some simpler kind of palpating machine than ours?

No, really directly . . . I see I'll have to demonstrate. Come here. Put your hand on my wrist—right on it, skin to skin.

May I really, Sir?

Yes, yes: no-one's looking. Now in the old days, if you were the doctor and I the patient, that would have been the usual thing. Television wasn't used in medicine at all; you wouldn't have been lying in your helicopter; you'd have been sitting close by your patient, probably in his home.

Sitting? Home?

Let's leave those words for another time, and return to auscultation. Doctors used to listen to the air going in and out of their patients' lungs, and the heart valves opening and closing.

How could they *hear* such things?

The world was virtually silent. Ancient literature is full of references to people's hearing the songs of birds and the cries of infants, and most authorities believe that such sounds literally were heard. The loudspeakers used to be turned off at night. Much of the Earth's surface was not even wired for sound. Probably everyone spoke much more quietly, and the way we are talking now would have been called shouting.

Shouting?

Speaking more loudly than is necessary.

But it is always necessary—

—To speak as loudly as possible. Yes, but it used not to be. What is more, in order to hear the lung sounds and heart sounds better, doctors used something called a stethoscope.

What was that like?

Nobody knows.

Is it true, Sir, that in those days patients used to do much better?

Do much better?

I mean, for example, was the recovery-rate from acute infections and trauma much higher? Did far fewer patients die in hospital?

It is quite true, and the reason is simple. Microorganisms were much less virulent then.

And what about trauma?

It used to be much less violent. No other explanation is possible.

How do you know all this, Sir?

Between ourselves, I've learnt to read. I know it's frowned on as taking up time which ought to be spent on listening and learning, and certainly you young fellows have enough to listen to; but you'd be surprised what interesting things have never been electronically recorded.

Can you write, too, Sir?

Aha, my boy, now you're pulling my leg.

* * *

When I decided to become a plastic surgeon (which was after I had decided to become a general practitioner rather than a psychiatrist, and before I decided to become an anæsthetist) I bought a special needle-holder and forceps. Anyone who has learnt to suture a wound with these tools will be unhappy using others, and they are useful in almost any medical career. Thus when I was sent, soon afterwards, by one of the Armed Services to the Middle East as Medical Officer With Special Training in Tropical Medicine (my capitals) I found my instruments useful in the treatment of men who had fallen foul of tent-pegs in the dark and of officers who had fallen foul of each other in the officers'-mess bar. Later I decided to become a cardiologist, and was appointed resident at Johns Hopkins. This turned out to be not Johns Hopkins in Baltimore but Johns Hopkins Memorial Agricultural College Students' Infirmary (their capitals) in a remote State in the Middle West. My instruments were here very useful in the treatment of skiing and skating injuries, and (in the brief summer) after lacrosse matches with the local Apaches. I then decided to become a writer, and I must confess that my instruments lay idle while I wore out several typewriters on my great gothic novel; but when the typescript was complete I found the forceps indispensable in getting the tape that was meant to hold the pages together to go through the tunnel formed by the tiny holes I had punched in each page (if any publisher happens to read this, I am still ready to consider offers for my novel). Then I decided to become a radiologist, and polished up my instruments again in the expectation of being able to sew up the skin after cutting down on an artery to perform an angiogram; but my ideas were outdated, for today percutaneous puncture is preferred to a cut-down, and even this (in the highly specialised country where I am being trained) is done by a surgeon, not a radiologist. So for the present my well-made, well cared-for, and experienced instruments are resting (if any young plastic surgeon, not yet fully equipped, chances to read this . . .)

* * *

The representative of the drug firm had a bad cold caught a couple of counties away; but, alas and alack, he had given away the last of his cold-curing samples just before the prodromal symptoms appeared. This was particularly sad, for his preparation of some new stuff—plus quinine, faith, and hope—would undoubtedly have prevented, aborted, cut short, or at least minimised to a triviality his streamer. Scrabbling in the drawer where I keep the samples left by his colleagues I was lucky enough to find the very wonder-worker he was talking about, neglected since his last visit. I handed it back as a practical expression of my sympathy, accompanied by my good wishes for a speedy recovery. He accepted it with a rueful laugh, and, entering into the spirit of the thing, watched while I ferreted out eleven other preparations to suck, sniff, squirt, ingest, or inhale—all highly spoken of by their compounders for their efficacy in his malady. He tucked them all into his bag saying that it would be something to talk about at the next meeting of his firm's reps.—assuming, of course, that he recovered.

* * *

From a coloured reproduction on sale at the National Gallery: Dürer, Albrecht (1471–1528)—The Painter's Father (before cleaning).

* * *

"Here's a stout little fellow sticking out all on his very own." His comb smartly tapped my polished cranium. Then his tune changed from the jocular to the regretful, "Dreadful. Oh, dear God, no. Ah no, broken off in his prime. Sheer murder. No life at all." Scissors and comb were placed with final emphasis by the basin. "Doctors [obviously he had spotted my pocket thermometer] should take more care of their appearance. All professional men should." "Well, I've still got my own teeth and don't wear glasses," I parried, staring below the level of his healthy glossy thatch into his rimless thick pebbles and the obvious upper and lower acrylics. But he went on reproachfully, "I could have helped long ago, perhaps, but of course a tight hat band——" "I never wear a hat." "That's the trouble. You should have worn a hat without a tight——." "I thought you said I had a tight scalp." "Never. Your scalp is loose, very loose. [He was confusing me now.] I said massage in your case would be a disaster. Breaks those tender little shoots. You massaged? Now all you've got is some fluff." He painlessly plucked a wilting but living hair from my occipital area. He was gaining the upper hand. "I never massaged. I spent a lot of time and money putting muck on." He raised his wispy eyebrows. "You rubbed it in?" "I certainly did." Triumphantly: "That's MASSAGE . . . I can see, sir, you need help; for instance I'm not ashamed to wear a mat." "What on earth——?" "A toupé, or rug as we call it in the trade, would suit you. All right, you don't want to be helped. Pity. Good day, sir. Thank you, sir."

* * *

The world is so full of a number of things
That I loathe the whole lot when the telephone rings.

Letters to the Editor

TROPICAL EOSINOPHILIA

SIR,—Those who are interested in filariasis have, for some time past, been impressed by the gradual and progressive unravelling of the basic ætiology of tropical eosinophilia.

The paper by Professor Webb and his colleagues in your issue of April 16 has taken us a long way to the solving of this problem, and in this solution the workers are to be congratulated. It therefore has now been definitely established that the common type of tropical eosinophilia is really a form of filariasis, most probably of zoonotic origin, and that, on this account, this entity becomes the prototype of what P. C. Beaver has so aptly termed visceral larva migrans.

As one who has been interested in the pathology of human filariasis for many years, may I comment upon the excellent photomicrographs which illuminate the paper in question?

They illustrate the cell-aggregation which constitutes the cell picture of human somatic filariasis and agree almost exactly with similar preparations made by T. J. Danaraj,[1] so that this combination of granuloma, eosinophil aggregation, epithelioid and giant cells, together with the hyaline acidophilic substance, referred to as M.K. (Meyers-Kouwenaar) bodies, constitutes the hallmark of filarial lesions in the lungs, liver, and lymph-nodes in the human body. These may now be taken as indicating the graveyards of embryonic and adult filariæ in the tissues and should be identified as such in the future. There is a cell-aggregation peculiar to filariasis, just as has been established for tuberculosis and leprosy.

May I be permitted to point out that this cell picture was originally described and figured by me in my *Report on Filariasis and Elephantiasis in Fiji* in 1912 (plates XXV, XXVIII, and XXXII). At that time it was thought that the cellular response was a reaction to the presence of the adult *Wuchereria bancrofti*, especially when defunct and calcified.

Subsequently, O'Connor and Hulse [2] in 1935 found that this reaction was provoked by dying or recently defunct microfilariæ in the lymph-nodes and other tissues, and their pathological preparations of the typical reaction produced by the embryo and adult filariæ have never been surpassed. They did not differentiate between the cell reactions in both cases.

Delving into the records of the past it is obvious that the best and most minute description of the pathology of human filariasis is to be found in the very excellent study by Wartman [3] in 1947 (Filariasis in American Armed Forces in World War II). The detailed descriptions of the pathological findings in biopsies from various sites occupy some 61 pages and remain undoubtedly the best ever produced. Some attention is paid to a comparison of tissue reactions associated with the presence of adult filariæ and that of the embryonic forms, or microfilariæ. In the former instance there is precipitation of strikingly acidophilic material around the remains of the worm with necrosis of tissue, exudation of eosinophils, plasma cells, lymphocytes, proliferation of macrophages and reticular fibres. In the case of microfilariæ, either defunct or calcified in the tissues, there is no necrosis and the precipitate around the embryos, when it occurs, is amphoteric. Œdema is conspicuous and the exudate consists chiefly of eosinophils. Macrophage and giant cells, although present, are not numerous and there is only slight reticular hyperplasia.

It can readily be realised that there exists a mass of long-standing observations which support the pathological evidence put forward by Professor Webb and his colleagues.

London, W.1. PHILIP MANSON-BAHR.

1. Danaraj, T. J. *Amer. J. trop. Med. Hyg.* 1959, **8**, 151.
2. O'Connor, F. W., Hulse, C. R. *Puerto Rico J. publ. Hlth Trop. Med.* 1935, **2**, 167.
3. Wartmann, W. B. *Medicine*, 1947, **26**, 333.

PLACENTA PRÆVIA

SIR,—In his admirable paper of Feb. 27 Professor Macafee refers to my condemnation of the use of Willett's scalp forceps in treatment.

In my paper [1] I reported two cases of maternal infection by the Welch bacillus, one of them fatal, following its use. I stated that "the risk increases with the length of time elapsing between the application of the forceps and delivery" and that "possibly if delivery took place within an hour or two of the application there would be little danger". One can only be reasonably sure that delivery will take place "within an hour or two" if the patient is in labour and the os dilating before artificial rupture of the membranes is done. Rupture of the forewaters plus a fundal binder will then generally allow the presenting part to be pushed down on to the bleeding point by the contracting uterus alone. This point is important as it is only during a contraction that bleeding in placenta prævia occurs. If this does not stop bleeding then I am all in favour of applying Willett's forceps and gentle traction on the forceps if and when bleeding recurs, and have advocated that in my book *Ante-natal and Post-natal Care*. If the membranes are ruptured artificially before labour starts the patient may not go into labour for some days even with the help of an oxytocin drip.

I do not think it necessary to terminate pregnancy routinely in cases of antepartum hæmorrhage at the 37th or 38th week, as Professor Macafee advises. I have always allowed these patients to go into labour spontaneously and have never had cause to regret doing so. This non-interference reduces the number of cæsarean sections and premature babies, and tends to prevent the difficulties that Professor Macafee has met with during the lower segment operation—namely, a poorly developed lower uterine segment "behind the symphysis making its exposure difficult". I strongly advise letting patients with antepartum hæmorrhage continue their pregnancy till the spontaneous onset of labour unless, of course, severe bleeding starts or persists, which at any time in pregnancy contra-indicates expectant treatment or its continuation.

I fully support Professor Macafee in his rejection of the use of placentography in antepartum hæmorrhage. After all he got his unequalled results in placenta prævia without its use.

Sydney. F. J. BROWNE.

SIR,—It was interesting to read Mr. Theobald's letter (April 23) recounting his experiences of obstetrics with drastic restriction in the use of X-rays. His excellent figures pay tribute probably more to his considerable clinical skill and experience and overall direction than to any one particular technique, giving support to the contention that it is not so much what is done as by whom it is done that matters. Yet surely it is far too early after only nineteen months to say whether or not the complete abandonment of skilled obstetric radiology is good policy in the long run.

It is true that in the past few years there has been concern about the possible risks of antenatal X-rays and I think most obstetricians, quite rightly, took the opportunity of reducing unnecessary radiography. Now that all the evidence is against such risks with ordinary care, it is surely out of place to try to perpetuate what, after all, was a temporary precautionary measure. It would be a tragedy if all that has been done for obstetrics by radiology were lost and the training of obstetric radiologists abandoned because of this temporary scare.

Mr. Theobald has lost no mothers from omitting placentography and pelvimetry and he "does not think" he has lost any babies. It is a pity he is not able to be precise on this point, for it is really in helping to reduce the *fœtal* risk that obstetric radiology can play such a big part in making breech and forceps deliveries safer; in diagnosing placenta prævia in the *ante* hæmorrhage stage and so helping expectant management for the

1. *Proc. R. Soc. Med.* 1930, **32**, 1209.

sake of the fœtus; in quickly freeing antenatal beds in mild antepartum hæmorrhage cases so that pre-eclamptic toxæmia can be treated properly and add to the chances of the fœtus. Again, when it was decided to give up radiography we are not told what new safeguards had to be taken—more routine work thrown on the consultant; more patients occupying precious obstetric beds; perhaps more transfusions. It is the precise answer to these issues that is needed before a strong argument can be put for the wholesale abandonment of radiography.

There is no doubt that in the recent past too many patients were being X-rayed, but reason should now prevail and allow selective radiography to continue playing its important part in the advancement of obstetrics.

ROBERT PERCIVAL
STANLEY MURRAY.

The London Hospital,
London, E.1.

ADDICTION TO DRUGS

SIR,—Your annotation of March 12 quotes the greatly respected American authority Dr. Harris Isbell. The opening statement, a reference to 50,000 drug addicts in New York City *alone*, may be misleading.

The best available evidence indicates that that is a considerable overstatement. The opiate addiction count is perhaps not more than 25,000 in New York City. Furthermore, a statement of addiction count in New York is likely to give a mistaken impression of the nationwide problem here. The addict count in New York may be little better indication of the addiction problem as a whole in this country than is the 150,000 to 250,000 addict count in Hong Kong a reflection of the addiction situation which might exist in the United Kingdom.

Opiate addiction in the United States of America is now confined pretty generally to the States of New York, California, Illinois, and Michigan, and the total addict count is perhaps somewhat less than 60,000. We stress this because American narcotic law enforcement is being plagued with a rash of publicity to the effect that in England, which never had a narcotic problem of consequence—even in the early 1920s when 1 out of every 400 Americans was addicted—there is the answer to our narcotic problem. England is being cited as possessing some magic alchemy for the control of narcotic addiction; all this to the derogation of the American attempts to control its narcotic problem.

The statement is being freely made here—and apparently through repetition it has achieved some acceptability—that the United Kingdom has no opiate problem because there narcotics are freely dispensed by doctors to all askers!

M. L. HARNEY
Formerly Assistant to U.S. Commissioner of Narcotics; Assistant to Secretary, U.S. Treasury, for Law Enforcement; Superintendent, Illinois Division of Narcotic Control.

Washington, D.C.

ADENOVIRUS TYPE-15 INFECTION

SIR,—We were very interested in Dr. Duncan's letter of April 9 on the isolation of adenovirus type-15 from 2 patients in Great Britain, since virus strains of this type were also isolated from 3 patients in The Netherlands.

A 4-year-old girl who was admitted to this hospital in January, 1957, with relapsing cystitis, developed a febrile pharyngitis two weeks after admission. Adenovirus type-15 was isolated from her fæces obtained on the fourth day of the respiratory illness.[1] The isolation was made in cultures of HeLa cells. Serum specimens were collected on the second day of illness and five weeks later. The patient showed a 16-fold increase in complement-fixing antibody against adenovirus type-4. No neutralising antibody for the prototype strain of adenovirus type-15 could be detected either in the acute serum specimen or in the convalescent specimen. However, a significant (128-fold) rise in neutralising antibody against the patient's own virus strain was found. Three rabbits were immunised with the prototype strain of type-15 and 3 rabbits with the strain isolated in this laboratory. The rabbit antisera showed reciprocal cross-neutralisation against both these viruses, but the neutralisation titres against the new strain were always greater (4 to 16 times) than those against the prototype strain.

The second patient from whom the virus was isolated in this laboratory was an 8-year-old girl who was operated on for appendicitis in January, 1958. A macroscopically normal appendix was removed. Signs of a previous ulcerative inflammation were observed on pathological examination. Fragments of appendix tissue were cultivated in test-tubes and showed a cytopathological effect after an incubation period of about four weeks. The cytopathological agent was identified as adenovirus type-15.

In January, 1959, an adenovirus was isolated by Dr. J. G. Kapsenberg in Utrecht from the stool of a 2-year-old girl suffering from mumps meningoencephalitis. The strain was sent to us to be typed and was found to be type-15.

1. van der Ploeg, G. Infecties met adeno-virussen bij kinderen. Thesis, Nijmegen, 1959.

Department of Bacteriology and Virology,
R.K. University,
St. Elisabeth-Hospital,
Tilburg, The Netherlands.

J. VAN DER VEEN
G. VAN DER PLOEG.

EXPIRED-AIR RESUSCITATION

SIR,—Thanks to addresses and articles such as those published recently in *The Lancet* and other journals in this country, in the United States, and in Scandinavia, " mouth-to-mouth breathing ", or to use a more euphonious term, expired-air ventilation, has made an impressive return to favour.

But, as so often, what appears to be excellent to some causes a clear, and at times almost violent, reaction in others. There are, of course, many problems associated with the looked-for introduction of a really effective method of artificial respiration, such as expired-air ventilation seems to be. Among the criticisms often heard are the following:

(1) *The supine position.*—Anæsthetists tremble lest the airway becomes obstructed with a patient lying prone, yet laymen are invited to believe that it is readily maintained in such methods as the Holger-Neilsen. As experts have said, however, the arms can too easily slip from under the forehead, and thus lead to airway obstruction. Strongly in favour of any position other than prone is that a movement of the chest can be seen by a rescuer; thus there is a constant check of the efficiency of the breathing.

(2) *Air is blown into the stomach.*—This rarely occurs if the airway is clear and the pressure less than 20 cm. of water: furthermore it is no great hazard, as it can be readily expressed.

(3) *Unhygienic.*—Surely yes! If the would-be rescuer has some foul infection of mouth or lungs, it may possibly be transmitted: this calls rather for selection of first-aid personnel than a wholesale condemnation of the method. We do not ban barbiturates because a collection of the capsules is so fondly cherished by would-be suicides.

(4) *Unæsthetic.*—So was going into the road with a dust pan and brush to collect manure for the garden. That was for the garden: this may save a child's life.

(5) *The rescuer's carbon-dioxide falls.*—Further experiments are being undertaken to verify that many people can greatly increase their minute volume without dizziness so long as they deepen and slow respiration. This calls for training (see below).

(6) *Instrumentation.*—Anæsthetists do not *always* choose the right size of airway from the wide range available! So the long anæsthetic type of airway should not be offered to first-aid personnel. Shortened airways, mouth props, rebreathing tubes with one-way valves, and so on are being introduced and may well be of real value for training purposes and for the use of experienced rescue teams. Simplicity and speed must ever be

the keynotes of success; valuable time may be lost while trying to find and fit a standard airway into a substandard mouth!

(7) *Training cannot be done.*—The essence of all methods of artificial respiration is to obtain and maintain a clear airway so that the adequate air can be made to pass into and out of the lungs. Surely techniques of training method can be worked out, short of the actual breathing into the victim. This is indeed the "difficult which can (and should be) done immediately". The impossible—practice manikins—will take a little longer. It is hoped that good-quality manikins will soon become available as it appears that they must form an integral part in any comprehensive training scheme.

In conclusion, I would quote from a letter recently received: "There are drawbacks to mouth-to-mouth breathing; there are advantages in the Holger-Neilsen: but it seems to me that there is one vital difference between the two methods—Holger-Neilsen does not work, mouth-to-mouth does."

Barnet General Hospital,
Barnet, Herts. ERIC K. GARDNER.

HÆMOGLOBIN STANDARD

SIR,—The letter by Dr. Stallybrass (April 16) calls for some comment.

First, no Commission can standardise the iron content of hæmoglobin. This is a quantity which is determined by practical experiment, and for human hæmoglobin, the majority of results obtained by professional scientists lie between the limits of 0·335% and 0·338% of iron in the compound.

Secondly, any Commission is entitled to express its opinion on the relative merits of the various results, but one which gave a recommendation that "100% Haldane became equivalent to an iron content of 14·6 g. per 100 ml." should be sent to the local cat's home with a shilling in its pocket. Apart from the confusion between "content" and "concentration" which is so commonly made that it almost passes as correct nowadays, it has apparently failed to realise the difference between a concentration of *iron* and a concentration of *hæmoglobin*.

Thirdly, the expressing of hæmoglobin concentrations as a "% Haldane" (or as a % anything else) is a very ancient method of recording chemical analyses. We still retain it as an old friend, in the same way that we continue to give a "quarter of morphine" instead of the more "refined" 16·2 mg. of that chemical.

Finally, the expression "100% hæmoglobin" can mean anything that one wants it to mean. No individual or Commission can lay down the law on the matter. It means one thing in Edinburgh; another thing in Lagos. But what is far more important is that "100% hæmoglobin" differs vastly between the two sexes in adult subjects, and this difference is almost invariably ignored. If "100% hæmoglobin" for males is taken as 14·8 g. hæmoglobin per 100 ml. blood, then "100% hæmoglobin" for females will be about 13·3 g. per 100 ml. This is unfortunate, but true.

Department of Biochemistry,
Western Infirmary,
Glasgow. E. B. HENDRY.

*** Dr. Stallybrass' last sentence should have read: ". . . what pathologist can afford knowingly to expose himself either to the charge of individualism, or of nonconformity, or even (if it must be said) of being behind the times?" This appeared as ". . . the pathologist cannot afford . . ." and we apologise to him for this unintentional change. We showed him Dr. Hendry's letter and his reply follows.—ED.L.

SIR,—The purpose of my letter was to draw attention to the fact that 100% Haldane may be equivalent either to 14·6 or 14·8 g. hæmoglobin per 100 ml. of blood. It was my intention to be uncritical of others, and perhaps for this reason I failed to be sufficiently critical of myself; this is the explanation of the regrettable confusion in my introductory paragraph, where the iron content of pure hæmoglobin and the hæmoglobin concentration of blood seem to reflect on the wisdom of the Protein Commission, thereby exposing it to frivolous ridicule.

Also, my letter failed to convey the sense (and this error was not my own) that individualism, &c., could be valuable characteristics, and that resistance to change in a rapidly changing world did not in principle meet with my disapproval.

Hertford County Hospital,
Hertford. F. C. STALLYBRASS.

SPINAL INJURY INVOLVING THE JEJUNUM

SIR,—Rupture of the aorta may result from hyperextension injuries of the lumbar spine and has been described by Lichtblau and Wilson [1] after manipulation of the spine in the treatment of ankylosing spondylitis. They also described a case in which a lumbar intervertebral disc space was opened by 2·5 cm. as determined by radiology, without serious sequelæ. In the case reported below a violent hyperextension injury opened a lumbar disc space so far that a loop of bowel was trapped between the vertebral bodies.

A motor-cyclist aged 17 years attempted to take a right-hand bend at a speed estimated to be about 50 miles per hour. He made some error of judgment and lost control of his machine. He was thrown through the air and it is thought that he may have struck the stay wire of a nearby telegraph pole. He complained to helpers of severe generalised pain and died a few minutes after the accident.

Necropsy findings.—There was a general appearance of exsanguination and multiple abrasions on the limbs and face. There was a linear abrasion in the lumbar region which ran diagonally across the back. There was a compound fracture of the left external malleolus but no other fracture in the limbs. No abnormalities were found in the head, neck, or thorax. His head had been protected by a crash helmet. The peritoneal cavity was full of blood but there was no rupture of any of the intra-abdominal viscera. On attempting to remove the bowel it was found that a loop of jejunum, about 18 in (45 cm.) from the end of the duodenum, was gripped between the bodies of the third and fourth lumbar vertebræ. The loop ran mainly through the left side of the intervertebral space. The fracture line was perfectly transverse and was at the level of the upper border of the intervertebral disc. At this level there was a complete transverse rupture of the anterior longitudinal ligament, and the psoas muscles had been avulsed from their origins. The inferior vena cava was intact but the adventitia of the aorta showed a considerable extravasation of blood throughout its abdominal course. There was no loss of continuity of the aorta, but the left renal artery had been torn off at its origin leaving a large deficiency.

This injury was probably caused by hyperextension and flexion to the right. The abrasion on the back and the evidence of more violent disruption on the left side of the body supported this view. The hyperextension must have torn the anterior longitudinal ligament allowing wide opening of the disc space. The aorta may have been saved from complete rupture by slipping to the right of the vertebral bodies. This would increase the likelihood of damage to the left renal artery. The stretched anterior abdominal wall, forcing the intestines against the posterior abdominal wall, caused the loop of bowel to be trapped between the vertebral bodies as they came together again. Death followed from massive hæmorrhage.

I wish to thank the Director-General, R.A.F. Medical Services, for permission to publish this case and Air Commodore W. P. Stamm for reading the manuscript.

Royal Air Force Hospital,
Wroughton. A. KENNEDY.

1. Lichtblau, P. O., Wilson, P. D. *J. Bone Jt Surg.* 1956, **38A**, 123.

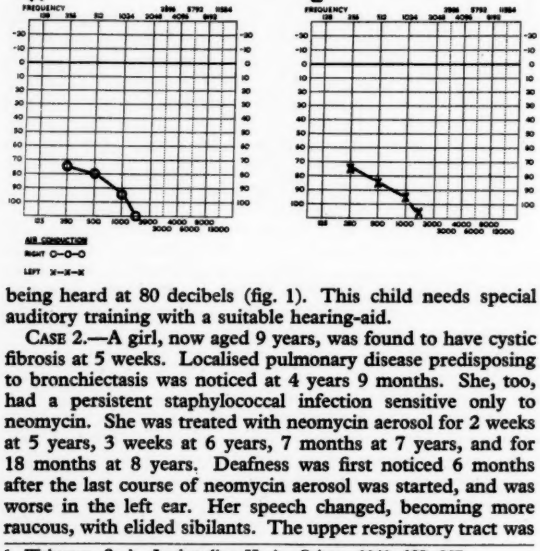
OTOTOXICITY OF NEOMYCIN AEROSOL

SIR,—Shortly after neomycin was introduced in 1949 [1] its toxic effect on the cochlea was described.[2 3] Damage to the cochlea followed systemic therapy particularly when there was renal dysfunction or concomitant damage to the kidney parenchyma. No case of deafness has been reported after topical application of neomycin. Costa [4] reported experimental observations on guineapigs treated with neomycin both systemically and by intranasal instillation; he only found cochlea damage in those given systemic neomycin.

The toxic action is confined to the cochlea. Experimentally it comprised atrophy or destruction of the organ of Corti [5] and degeneration of the stria vascularis and cochlea ganglion [6]; severe impairment of hearing was also demonstrated in animals without pathological changes in the organ of Corti.

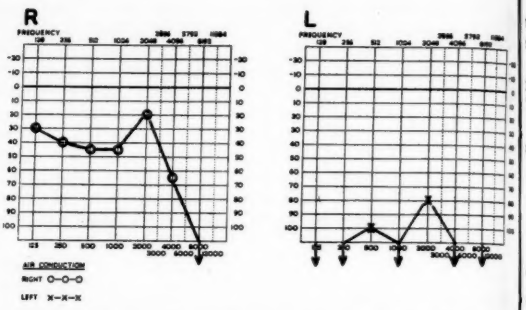
Ototoxic damage usually follows long-continued treatment, but it has arisen within 8 days.[2] In the two following cases deafness developed after neomycin aerosol had been given for 28 and 18 months. The deafness increases the longer neomycin therapy is continued, and unfortunately it tends to exert its action after the drug has been discontinued.[7 8]

CASE 1.—A girl, now aged 5 years, had been found at the age of 12 months to have cystic fibrosis associated with a persistent pulmonary staphylococcal infection, sensitive only to neomycin. This was given in aerosol form for 6 weeks when she was 21 months old, and for 28 months a year later. Deafness was first noticed at $4\frac{1}{2}$ years and it increased rapidly during the next 3 months. Until the deafness began her speech developed normally; it then degenerated rapidly into babbling, with a discordant voice. The upper respiratory tract showed no abnormality. Audiometry after conditioning showed a severe bilateral perceptive deafness, only low tones



being heard at 80 decibels (fig. 1). This child needs special auditory training with a suitable hearing-aid.

CASE 2.—A girl, now aged 9 years, was found to have cystic fibrosis at 5 weeks. Localised pulmonary disease predisposing to bronchiectasis was noticed at 4 years 9 months. She, too, had a persistent staphylococcal infection sensitive only to neomycin. She was treated with neomycin aerosol for 2 weeks at 5 years, 3 weeks at 6 years, 7 months at 7 years, and for 18 months at 8 years. Deafness was first noticed 6 months after the last course of neomycin aerosol was started, and was worse in the left ear. Her speech changed, becoming more raucous, with elided sibilants. The upper respiratory tract was



normal. Audiometry revealed no hearing in her left ear, and very severe high-tone perceptive deafness in the right ear (fig. 2). The hope of this child retaining her speech is greater than in case 1, because she is older and had acquired more speech before she became deaf. She has at present more useful hearing than has case 1.

I wish to thank Mr. N. Asherson for permission to describe these cases, and Dr. L. Fisch of the audiology unit for assistance in their examination.

Royal National Throat, Nose and Ear Hospital, Gray's Inn Road, London, W.C.1. ALAN FULLER.

NOTIFICATION OF UNSUCCESSFUL CANDIDATES

SIR,—Is there any reason why boards of governors and regional hospital boards should not tell candidates for appointments that they have not been short-listed as soon as this is known?

The common practice at present seems to be to wait until the appointment has been made before telling those candidates who were not interviewed that they have been unsuccessful. This practice results in prolonged doubt and anxiety for applicants which a little thoughtfulness could lessen. Sometimes other decisions, such as whether to apply for another job, may hang upon the result of an application; and if a man knows promptly that he has not been short-listed he can plan his affairs accordingly.

I write not out of a sense of personal grievance but because I have seen friends suffer emotional stress unnecessarily.

SUCCESSFUL APPLICANT.

INTERMITTENT POSITIVE-PRESSURE RESPIRATION IN INTRACTABLE STATUS ASTHMATICUS

SIR,—I congratulate Dr. Broom (April 23) on the successful resuscitation of the two cases of severe status asthmaticus.

I notice, however, from the case-history that both patients were given *on admission* intramuscular injections of chlorpromazine and promethazine, supplemented in one case by intramuscular pethidine. Three hours later one of the patients is reported as being "well sedated". Four hours later the patient was moribund. The other patient's condition deteriorated some two hours after the initial sedation and further chlorpromazine and promethazine was given for restlessness after another two hours. Four hours later the patient collapsed and became moribund.

I have always felt that the acknowledged ill-effects of opiates in patients with severe bronchospasm resulted not only from depression of the respiratory centre, but even more so from the induction of a dangerous mental state of "couldn't care less", with loss of will to fight for breath and to cough up sputum at the appropriate time.

Chlorpromazine and promethazine must induce just this mental state. It is difficult not to suspect that the sedatives contributed to the serious deterioration of the patients' state and

1. Waksman, S. A., Lechevalier, H. A. *Science*, 1949, **109**, 305.
2. Waisbren, B. A., Spink, W. W. *Ann. intern. Med.* 1950, **33**, 1099.
3. Carr, D. T., Pfuetze, K. H., Brown, H. A., Douglass, B. E., Karlson, A. G. *Amer. Rev. Tuberc.* 1951, **63**, 427.
4. Costa, F. *Arch. ital. Otol.* 1957, **65**, 233.
5. Hawkins, J. E., Jr., Rahway, N. J., Lurie, M. H. *Ann. Otol., &c., St. Louis*, 1953, **62**, 1128.
6. Riskaer, N., Christensen, E., Petersen, P. V., Weidman, H. *Acta oto-laryng., Stockh.* 1956, **46**, 137.
7. Havard, C. H. W., Garrod, L. P., Waterworth, P. M. *Brit. med. J.* 1959, i, 688.
8. Körtge-Stöppler, S., Mittag, G. *Münch. med. Wschr.* 1958, **100**, 1189.

that it would have been wiser to delay their use until bronchospasm was further relieved or at least to have used smaller doses.

Finally it would be instructive to know if the three cases of fatal asthma mentioned were also given the same initial sedation. The problem is an important and vital one.

It is hoped that the queries raised in this letter will be accepted as a constructive criticism, not a destructive one.

The Radcliffe Infirmary, Oxford. E. M. BUZZARD.

MEANING OF ANALGESIA

SIR,—I should like to make a plea that the word "analgesia" should be used to indicate what its origin clearly suggests—relief of pain. Its use to describe a block of nerves within the dura mater has for some time seemed awkward and leads to remarks such as "an alternative form of anæsthesia is spinal analgesia" and so on. Nerves that are adequately blocked cease to transmit all sensations, not only those of pain.

But much more serious is the misuse of the word to cover all the drugs that are given to ease the pains of labour. Under the term "obstetric analgesia" one finds descriptions of all sorts of drugs, many having no analgesic properties. Drugs such as, for example, tranquillisers may make a mother feel better; they may make her feel worse. There are some mothers who, though they welcome analgesia, dislike very much the feeling of dissociation, of losing possession of themselves, which such drugs may produce. It is possible to stretch a point and say that tranquillisers can in some cases relieve mental pain. Equally, they can block an approach to the causes of this pain. In any case, in order to use drugs most effectively for easing pain in labour the administrator should be reasonably clear in his mind what actions he is expecting from them.

University College Obstetric Hospital, London, W.C.1. SHÎLA RANSOM.

"ELECTROPHEROGRAM"

SIR,—Gerrits et al.[1] have referred to "some deviations of the serum-protein spectrum and curve (electropherogram) in patients with pulmonary carcinoma".

The word "electropherogram" as used by these authors appears to mean the densitometric or colorimetric pattern obtained from filterpaper strips on which serum has been electrophoretically separated and stained. Such connotation is not universal since other investigators [2] also refer to stained electrophoretic strips as "electropherograms". In addition, there is a lack of uniformity in the spelling of apparently the same term. Talluto et al.[3] use the word "electrophoreogram" while Zak et al.[4] discuss the stained pattern of an "electrophoretogram". Furthermore, other workers have shortened the expression to "pherogram" [5] or "electrogram".[6]

This term as used in the literature can designate a number of different products of the electrophoretic process which are by no means equivalent. When the word "electropherogram" or a variation thereof is used, a definition should be included in the text to avoid ambiguity. The value of terminology per se depends largely on its specificity. Therefore, to prevent confusion the formulation of a more definitive nomenclature pertaining to electrophoresis may be indicated.

Departments of Pathology, Los Angeles County Osteopathic Hospital, College of Osteopathic Physicians and Surgeons, Los Angeles. R. L. SEARCY L. M. BERGQUIST.

1. Gerrits, J. C., Stolk, A., Verleur, H. L. *Lancet*, 1959, i, 470.
2. Stern, J. R., Mais, R. F., Boggs, G. D. *Clin. Chem.* 1957, **3**, 599.
3. Talluto, K. F., Benerito, R. R., Singleton, W. S. *Analyt. Chem.* 1958, **30**, 1059.
4. Zak, B., Jarkowski, T. L., Williams, L. A. *Amer. J. clin. Path.* 1959, **31**, 599.
5. Wieme, R. J. *Clin. chim. acta*, 1959, **4**, 317.
6. Hakim, A. A. *ibid.* p. 484.

THE SHORTAGE OF NURSES

SIR,—In his letter last week Mr. Malkin has made some constructive suggestions about the present serious shortage of nurses. This problem is closely associated with a grave and increasing shortage of hospital resident staff, and a great deal of the extra strain imposed on nurses is caused by unfilled, or inadequately filled, resident medical posts. Many nurses are, in fact, carrying out duties which properly lie within the province of house-physicians and house-surgeons. For this they get no recognition, and resentment at this state of affairs I am sure is increasing.

Hospital practice conditions have changed tremendously since the inception of the National Health Service, and we must now realise that many resident medical posts in hospitals will not in future be filled. Plans to continue our work must be made, possibly with the help of some form of technical assistant. The Aftercare Sister, common at one time in orthopædic practice, is a very valuable person with much greater knowledge of the technicalities of orthopædic surgery than any newly qualified doctor. She is, in fact, a recognised technical assistant, and handles alone without the presence of any doctor a form of clinic well known to orthopædic surgeons.

The two problems—shortage of nurses and shortage of resident staff—should, I suggest, be considered together. A central body consisting of representatives of the Ministry of Health, the hospitals, the British Medical Association, and the Royal College of Nursing, as proposed by Mr. Malkin, seems ideally constituted for this purpose. Within a short time of its formation the gravity of these two problems would be appreciated much more widely than at present. The necessity for action to change our present system would be realised, and certain steps to improve the situation might soon become obvious. The matter is certainly urgent.

Northampton. W. R. D. MITCHELL.

HUMAN RELATIONS IN OBSTETRIC PRACTICE

SIR,—As a psychiatrist I should like to express my complete agreement with Professor Morris (April 23).

When my wife was having her fourth child the obstetric surgeon said she should have it in hospital as she had a moderate macrocytic anæmia of pregnancy, but after I had seen the unit and sensed the impersonal and unsympathetic attitude of the sister-in-charge, who clearly resented my desire to see where my wife would have her baby, I preferred to risk a P.P.H. at home.

Both friends and patients have many times told me of not only the absurd rituals they have had to endure but of the way their feelings have been disregarded and their opinions and wishes ignored.

The fault lies primarily, I think, with the obstetricians. The majority of them are not sufficiently interested in the emotional feelings of their patients—if they were they would be as concerned as psychiatrists are at the present time to create a permissively relaxed and friendly atmosphere in their units, and this is clearly not the case. In addition their treatment of women in gynæcological clinics is, so often, inhumanly impersonal and even occasionally brutal.

The reproductive organs of women are of profound and deep psychological significance. It is no accident that hysterectomy is a profoundly disturbing emotional experience to many women, an experience and trauma for which they should be prepared not only by explanation and reassurance but also by a friendly and understanding approach by all the staff of the unit.

After the birth of my first child my wife was seen by an eminent gynæcologist for some degree of prolapse. His psychological approach was appallingly cold and indifferent. As he is

a teacher and an examiner there must be many obstetricians and gynæcologists who, having passed through his hands, are not very likely to have been taught to appreciate the emotional needs of their patients.

I believe much minor and some major psychological illness (particularly depression following hysterectomy) in women could be prevented if obstetricians and gynæcologists showed real understanding for their patients and tenderness in their approach. Ten minutes of explanation and reassurance in a unit where all the staff understand the principles of permissive psychotherapy in a non-authoritarian setting will prevent years of unhappiness and perhaps hours of a psychiatrist's time at a later date.

Far more emphasis on the emotional needs of patients and some understanding of the unconscious factors that lead to fears and anxieties about conception, childbirth, and gynæcological operations must be given to the doctors and nurses in training. Nevertheless I am afraid this will not entirely solve the problem, for there is no doubt that so much of the prevailing punitive attitude toward pregnant women is the projection on to the prospective mother of the unresolved conflicts concerning sex in the minds of the doctor and nurse, especially the senior hospital midwife. There is no doubt that many of these women are deeply jealous (often at an unconscious level) of their patients' ability to have children, and perhaps need to be made aware of their unconscious attitudes.

The Towers Hospital,
Humberstone, Leicester. H. B. KIDD.

LONG-ACTING SULPHONAMIDES AND PROTEIN-BINDING

SIR,—The paper by Mr. Newbould and Dr. Kilpatrick (April 23) is of considerable topical interest, since it reports a study of two new and widely used long-acting sulphonamides—sulphaphenylpyrazole (' Orisulf ') and sulphamethoxypyridazine (' Lederkyn '). The compounds are compared with two well-established sulphonamides—sulphadimidine and sulphadiazine.

The methods used and the observations made are described in detail and with great clarity. The authors have with commendable scientific restraint refrained from drawing firm conclusions from their results. In view of this restraint, it seems particularly unfortunate that two statements appear in the paper which, as they stand, may mislead. I should therefore appreciate the opportunity of drawing attention to them.

(*a*) In the second paragraph of the preamble in reference to the two sulphonamides studied: " Though in-vitro these compounds had similar anti-bacterial activity to sulphadiazine, some of the results of clinical trials were disappointing (Harris et al. 1957, Prlina et al. 1958). Better results were claimed when larger doses were used (Walker and Hambukger 1957, Grieble and Jackson 1958, Jefferson 1958)."

(*b*) In the paragraph immediately preceding the summary on p. 891: " Toxic effects with these newer drugs have already been described (Holsinger et al. 1958, Lindsay et al. 1958, Schwartz and Norton 1958) and if larger doses have to be employed for therapeutic activity the patient may be exposed to a greater risk than that associated with sulphadimidine."

Eight references relative to these sentences are given. In none of these is sulphaphenylpyrazole mentioned.

A feature of sulphaphenylpyrazole is its remarkable freedom from toxic effects. A leading article [1] in the *British Medical Journal* recently said:

" Pharmacological studies in man, confirming the prolonged action of this drug, were described by A. F. Essellier and his colleagues, by P. Rentchnick, who compared its behaviour with that of sulphamethoxypyridazine, and by D. Bachmann and his colleagues. All these authors also report good clinical results, perhaps the most enthusiastic paper being that by Essellier et al., since they claim success in the treatment of infections by bacteria most of which are said to have been sulphonamide-resistant, and in such conditions as chronic cholangitis and diverticulitis. One of the authors himself took 25 g. of sulphaphenylpyrazole daily for five days and experienced no ill effects—a bold demonstration of lack of toxicity."

1. *Brit. med. J.* 1959, ii, 482.

Ciba Laboratories Limited,
Horsham, Sussex. A. K. PITTMAN
Director of Clinical Research.

THE PERSONAL DOCTOR

SIR,—I trust Dr. Fox's article (April 2) will evoke the long, hard thinking it deserves and, I am sure, was intended to evoke, and I hope he will not be mistaken either for enemy to general practice or for a diehard conservative in need of a fresh demonstration by the sapient Canute. May I, as one lately retired from family and personal, if not general, practice, give some relevant evidence?

Beyond question the scope of general practice in the fields of medicine, surgery, and midwifery has contracted in the past 50 and perhaps especially in the past 20 years, most, no doubt, in the towns, but the country can hardly have escaped. Dr. James Mackenzie of Burnley, in the early years of the century, resecting loops of intestine and removing ovarian cysts in the intervals of unravelling the cardiac arrhythmias, could have thought me a sadly circumscribed specimen of general practitioner even 30 years ago, and if, in the last 10 years, he had chosen to say that I no longer deserved that proud title I could not have gainsaid him. There was no other name for me and my kind, but the number of things I no longer did for my patients increased, and to maintain birth-to-death continuous care became yearly harder. I am sure, too, that I was not alone in finding myself regrettably seldom the full, unquestioned doctor to the family I had so often been in earlier days. The disappearance of the nursing-home, so essential to continuous care in the type of practice prevailing in the neighbourhood, seems to prove that what happened to me happened also to my neighbours. In fact general practice and family practice have unquestionably been on the wane in the " residential area " of London about which alone I am qualified to speak. The term " personal doctor " would describe my professional occupation fairly accurately in the past five to ten years.

On the other hand I can and do vouch for it that in the field of " personal medicine " there has been no lack of work and that many patients, diverse in age, sex, occupation, and native land, do still find a use for a doctor " living over the shop ", visiting them, when convenient or needful, in their homes, or listening to them, examining, advising, and medically ministering to them in a consulting-room furnished and equipped to his individual taste and expressing something of his personality. " I do like this room," they have said—as they might say of the consulting-rooms of many of my medical neighbours; and I am certain that, in a room they actively like, patients are more ready to give a history fully and without reservations, to ask the questions they ought to ask, and to listen to and accept advice; they are also—young ones especially—less likely to be frightened.

Sometimes I fear the personal doctor is doomed, as Dr. Ashworth so cheerfully and confidently prophesies, and that the citizens of the future will have a team or a clinic for his doctor. It could very easily happen. That blind, unreasoning power " the spirit of the age " perhaps still favours it, and if it is not to happen those who believe that something good would have perished must stand, individually and collectively, for their faith. If they want a little encouragement and Dr. Ashworth wants food for thought it is provided only 15 pages before his letter in your issue of April 23 where Dr. Norman Morris, writing of Human Relations in Obstetric Practice, quotes the

opinions of some expectant mothers on some antenatal clinics. Quite clearly they needed a personal doctor. I hope—*how* I hope—that in this country it will never be impossible for them to get one.

Crockham Hill, Edenbridge, Kent. LINDSEY W. BATTEN.

SIR,—I should like to support Dr. Fox's contention that the general "comprehensive" practitioner, as such, no longer exists in this country. I would also support his view that his successor is equally important. His function must therefore be defined in clear terms. May I take up some points raised in the correspondence following Dr. Fox's article?

General comprehensive practice does exist and is not hypothetical as stated by Dr. Hunt (April 9). An Australian friend described practice on a bush station where he was responsible for treating acute nephritis, trephining a skull, or doing a cæsarean section, and did so if necessary. In other remote and isolated parts of the world many doctors are still doing quite complicated surgery and obstetrics as well as dealing with general medicine, psychiatry, and minor surgery. This type of practice, properly termed general practice, was widely done in the nineteenth century in this country and has declined in this century to the present state of affairs where the general practitioner is no longer general in this original sense. Medical schools have contributed to this decline, and the consequent decline in esteem, by emphasis on specialisation and horrific accounts of G.P.s' mistakes—e.g., removal of both ovaries from young women because of simple cysts found at operation for appendicitis. I do not know on what evidence Dr. Hunt implies that general practice, even as defined by him, has been in existence for thousands of years. The only evidence that he gives in the time of Hippocrates is to the contrary. In modern times the barber-surgeon, physician, and apothecary were quite distinct, and I suspect that their functions were only brought together to create the general practitioner within the past two or three hundred years.

It is as important for a specialist to have a general background as for a general practitioner. Otherwise we shall have the worst kind of specialist. Conversely the minute study of a small aspect of a special branch of medicine can deepen the understanding of medicine as a whole and of medical research, for those who are or will become general "personal" practitioners.

In answer to Dr. Ashworth (April 23), who thinks that a team should take over the family doctor's function, I would say that a personal doctor can still make use of nurses, receptionists, and laboratory aids (an extension of physical examination) as I do in my practice and at the same time preserve the individual personal relationship. There is also no inherent reason why physical and psychiatric preventive medicine should not be carried out from the doctor's own surgery. Most doctors of my acquaintance already undertake antenatal care and many fully immunise their patients.

Having spent a year as a medical resident in a hospital in the United States I can confirm the tendency towards specialisation and towards the internist becoming the personal family doctor. The latter process often leads to the internist having inadequate experience to remain expert in his specialty. As an erstwhile medical registrar and present general practitioner and having had relatives needing close medical attention, my experience confirms the need for a personal doctor who will advise the patient on every aspect of health. Whenever he feels competent, he should deal with the problem himself.

Until the change in general practice is fully appreciated by the medical profession in this country, it is difficult to see how any positive approach to the definition of this essential aspect of medicine can be made. Without this definition any great advance or regeneration is unlikely to take place. This is not to say that there are no good general practitioners in this country. But from most accounts regenerating forces are badly needed in some areas.

Cambridge. B. B. REISS.

SIR,—I enjoyed Mr. Malcolm Donaldson's letter of April 30, but if he will re-read mine he will see that I referred not to those who bellyached, but to those who bellyached about trivialia—an entirely different category.

I should like also to explode this myth of the "overworked" doctor. If a G.P. nowadays is overworked he is either unmethodical or has too large a list, or both.

Crediton, Devon. L. N. JACKSON.

THE LATE DR. JAMES BROWN: A MEMORIAL LIBRARY

Dr. D. VEREL, of the Sheffield Region Cardiovascular Centre, City General Hospital, Sheffield, 5, writes:

"Friends of the late Dr. James Brown may like to know that his large collection of journals and cardiological reference books has been given to the department he founded to form a memorial library. The majority of the journals have now been bound and housed in his old department where they constitute an invaluable source of reference. A few issues of the cardiological journals are missing.

"It may be that some colleague would be willing to present to this library the missing issues so that the collection can be completed. The journals concerned are:

"*Archives des Maladies du Cœur et des Vaisseaux*, three numbers missing between 1940 and 1956; *American Heart Journal*, three numbers missing between 1940 and 1956; *Circulation*, October, 1958; *British Heart Journal*, July, no. 3, 1954.

"Oddly enough, in most cases where a journal is missing there exists a duplicate journal of the wrong month."

Parliament

Payment of the Doctor

IN opening the debate on the Pilkington report in the House of Lords on April 27, Lord MORAN posed two questions: why were the consultants, broadly speaking, content; and why were the general practitioners far from content? In his view the answer was that the principle of exceptional reward for exceptional merit was applied to one group but not to the other.

He recalled that, when the National Health Service began, the system of merit awards was introduced despite the opposition of the Treasury, the British Medical Association, and the universities, and the indifference of the consultants themselves. After ten years he believed that the position had completely altered. The Royal Colleges had always been behind the awards, but now the council and representative meeting of the B.M.A. were also unanimously in favour. The Treasury had said, "There is nothing like this in the public service, but it seems to work, and we hope it will go on." Both the majority and the minority reports of the Royal Commission said, "These awards are the one imaginative feature in the whole of the Health Act." As chairman of the Awards Committee he naturally welcomed this change in the climate of opinion. But though the Royal Commission had in principle approved of the awards system, they had, in Lord Moran's view, offered it disappointingly meagre practical support. The addition of £500 to the A award and £250 to the B award did not make up for the change in the value of money over the past ten years. A more serious criticism was that the number of awards, which in the past had increased as the number of consultants increased, had been frozen and fixed. If the number of consultants continued to increase at the present rate, this would mean that in

nine years time only 1 in 4 consultants, instead of as at present 1 in 3, would receive an award.

For the general practitioners, on the other hand, there had so far been no system of award, and to this lack Lord Moran firmly attributed their discontent. A general practitioner could add to his income only by increasing the number of his patients, and the present permitted maximum of 3500 was more than one man could look after. Many doctors with large lists had been hoping the Royal Commission would devise some means whereby a premium could be put on good work. The Royal Commission had responded by putting aside £500,000 and saying to the practitioners: "You can have this if you can evolve a system." The problem of devising a scheme which would keep the general practitioner on his toes was not easy, but Lord Moran hoped that we should not be "fobbed off with the suggestion that instead of merit awards there should be responsibility awards, so as to avoid all the unpleasantness of deciding who is meritorious and who is not". Responsibility was synonymous with seniority. Those who were senior would no doubt welcome a financial bonus as a solace to the handicaps of advancing years, but it would not pay the community. To introduce these awards somebody was needed (perhaps, say, a Lord Waverley) who could arrive at the answer to a question by first principles and then, having come to his conclusion, refuse to budge an inch, no matter what the opposition. We did not want a Gallup poll of the sections of the profession to see what they were thinking at any moment. This would be one man's job. It would be a creative act; and, like all creative acts, it had got to happen in the brain of one man.

Lord Moran believed that the proposal for a review body was essential because for medicine the Government were a monopoly employer. They controlled the demand, the supply, and the pay of doctors. Was it any wonder that the profession was apprehensive of some arbitrary action on the part of the Government? And nothing that had happened in the last ten years had been very reassuring. Doctors had lost all faith in the Whitley machinery. We needed something absolutely new, and he implored the Minister to set up something on the lines of the proposed review body. Here was a golden opportunity to win the confidence and faith of the profession and to start a new era in the relations between the profession and the Government.

ALTERNATIVES TO THE COMMISSION'S RECOMMENDATIONS

Lord TAYLOR agreed that the proposed standing review committee was vitally important for future wage relations and structure. He regretted all the more that it had already been decided that the review committee were not to have access to the information which the Board of Inland Revenue had about the earnings of doctors and dentists and about the earnings of other professions. To collect the necessary information by repeated detailed questionnaires to busy professional people might well prove impossible.

Of some of the other recommendations he was more critical. For instance, he considered the proposal in the minority report for an average net annual income for the general practitioner of £2550 to be more in accordance with trend of pay in other professions than the Commission's figure of £2425. The first ten years of the N.H.S. had clearly shown that the way in which a doctor is paid helped to determine the service he could give, and Lord Taylor's chief disappointment was that some of the Commission's recommendations would tend to work against the public interest. They described cash incentives to group practice as "somewhat excessive", and extra cash for rural doctors as "somewhat overdone". They doubted whether anyone was competent to set a top limit to the number of patients a doctor should have, yet the Ministry and the doctors between them had fixed in 1948 a limit of 4000 and, when the Danckwerts award came along, a limit of 3500. He agreed with Lord Moran that 3500 was still too high. Lord Taylor thought that when the Pilkington rates were introduced, despite the Commission's lack of directive, the opportunity should be taken to reduce the maximum permitted list to 3000.

The proposal for merit awards for general practitioners he dismissed, quite apart from its merits or demerits, as "out of this world". In his view nothing short of a two-day visit, living and working with a G.P., would enable one to assses his real quality and merit, and there were 22,000 general practitioners from whom the fortunate 750 must be selected. Instead of merit awards he proposed a differential for age. A general practitioner's income (unlike a consultant's) started to fall when he reached the fifties, for general practice was one of the toughest physical jobs. He proposed giving the G.P. over fifty an extra £50 a year for each year between fifty-one and sixty; so that at sixty a general practitioner would get an extra £450 a year. The supplement might be linked with a minimum list of say 1000. He estimated that it would cost just over £1 million a year, or twice the Royal Commission's figure of £500,000 for the differential awards. It would put right a manifest wrong and would reward those who had borne the heat and the burden of the day and give them a chance to ease up a little when most of us eased up, without financial detriment to themselves and their junior partners.

Lord Taylor was grateful to the Royal Commission for providing the first proper statistical analysis of the awards given to consultants. It showed that every consultant had a more than even chance of getting an award before he retired. He was sure that all who received awards deserved them but he was uneasy about the 45% who never achieved merit. The effect on them was wholly bad. Could we be sure that among them were not many who deserved as well of their patients and the nation as the fortunate 55%? He believed that ultimately we should be driven to the view that the only honest and right thing to do for the future was to amalgamate the C merit awards with the general consultants' salaries. The invidious process of selecting at this comparatively low level of merit would end, to the great benefit of general hospital morale. Two-thirds of the awards were rightly divided among the 2000 teaching-hospital consultants, and he suggested that in future the B awards should be amalgamated with the salaries of teaching-hospital consultants and special regional-hospital-board units. The effect would be much the same as at present, but the invidious process of choosing and excluding would go. In the face of this, there was no real justification for the proposed A-plus awards, and it would be better to increase the number of A awards to, say, 450. Most of the consultants with A awards were part-time. Their private practices were doing well, thanks to the boom. These proposals would cost the nation no more than the Royal Commission's proposals: the Awards Committee would have to pick out only the top 450 men and women from the profession, instead of 2800, as at present. Those who were appointed to special posts would automatically get special recognition. But the secret division of staffs within hospitals into better-paid sheep and worse-paid goats would cease.

THE REVIEW BODY

The Earl of DUNDEE, speaking for the Government, gave some information about the new review body. It had been asked how the Government would interpret the recommendation that the members of this body should be appointed after "consultation" with the professions. On the one hand, it would not be constitutionally proper that the medical professions should have a formal right of veto of any member to be appointed: but the Government recognised that this body would be no use if its members were not acceptable to the professions. The comments of the professions would be invited on a provisional list of members, and their views would be fully taken into account. The Government would do their best to see that the medical profession would be satisfied with the membership. They were also ready to give an undertaking that any representations which the professions wished to make to the Review Body would be passed on to it by the Government, including any suggestions that for some particular reason a review earlier than the normal minimum period of three years might be desirable. The Government recognised that the medical profession attached special importance to being able to present their arguments to the review body orally, and were prepared to make a recommendation to the

body that the professions should be given that opportunity if they wished to have it.

FURTHER DISCUSSION

Lord AMULREE, speaking as a part-time consultant, suggested that his colleagues, the whole-time consultants, laboured under some disadvantages, such as difficulty in getting allowances for travelling expenses to conferences, professional journals, and telephones. He welcomed the substantial increases for young hospital doctors but he trusted that this time almost all the increase would not be absorbed by an increase in the charge for their keep. He approved Lord Taylor's suggestion for a payment to elderly general practitioners. He would like to see the N.H.S. ensuring that the general practitioner had some leisure when he grew older.

Lord COHEN OF BIRKENHEAD supported the system of merit awards—"wholly illogical in theory, but it works"—and did not want to see it modified according to Lord Taylor's suggestions. But the present system had some anomalies, especially in universities, which he believed should be corrected. For instance, preclinical medical staff were not eligible for awards. He agreed that awards for general practitioners were desirable but doubted if they were practicable. Despite the unlikelihood of finding any other acceptable criteria than age and length of experience, he would like to see the proposal examined with a much larger sum in mind, so that not 1 general practitioner in 23 but perhaps 1 in 4 would receive an award. That might simplify the problem. But the least worthy reason for accepting the scheme was that it would be just another handful of silver for the kitty. If a scheme for awards could not be devised he would like to see the money used for other purposes—such as incentives to single-handed general practitioners to take holidays, or help to general practitioners disabled in the course of their service. He hoped that the Royal Commission would have been the beginning—and that the review body would be the continuation—of a machinery which would prevent the disputes, the manifestoes, and ultimatums which had from time to time been displayed in public; and that the brilliant history of the National Health Service would not be scarred in the future, as it had been in the past, by unseemly wrangles.

Baroness WOOTTON of ABINGER said that the Royal Commission had collected for the first time evidence about relative professional earnings. Her only regret was that they had not discussed its significance. Instead they had offered an ex-cathedra statement, with which she did not disagree, that doctors' earnings were too low. According to the Willink Committee, there was at present an adequate supply of medical students in training. A harsh and ruthless economist would have drawn the conclusion that the pay of doctors must therefore also be adequate. But the Royal Commission, discarding thereby the whole of economic learning, blandly took the view that this meant that there was no relevance in the conditions of supply, and they dismissed them out of hand. Nor did they substitute any alternative criterion, such as job analysis of the conditions of work of occupations that might compare with that of a doctor. Having abandoned economics and having abandoned work comparability, the Royal Committee were left in a vacuum. Thus the hierarchy of the profession as it stood would really be an expression of social conventions and of the values recognised and esteemed in our society. We had these conventions, but we did not discuss them. And the result was that we were gradually committing ourselves to an astonishing rigidity in the pattern of remuneration.

GOVERNMENT REPLY

Lord ST. OSWALD in ending the debate returned to the procedure of the review body. The Government had undertaken to ensure that the profession was fully consulted on that body's membership. They would also give a firm undertaking to pass on any recommendation made by the profession and to stress to the review body the importance attached by the profession to being able to present their case orally. He was aware that doctors and dentists would prefer to be able, so to speak, to "press the button" themselves to set this machinery in action, though some doctors were not happy that any "monopoly employer" should be within reach of the button. But that was not among the recommendations of the Royal Commission, and it was not favoured by the Government as a unique privilege for the medical profession. The recommendations, as accepted, contained acceptance of the exclusion of doctors and dentists in the composition of this body. Many doctors agreed that the position of professional delegates on the review body would be intolerable—that they would be blamed by their colleagues for every failure to act as a body as a whole or to act as the bulk of the profession. The Government were satisfied that it would not be practicable for the Inland Revenue to provide the review body with the information they required, and that body should be able to obtain it by other means. List size would be a matter for discussion in detail as part of the consideration of the distribution of the pool. Implementation of the report did not depend on the acceptance of merit awards for general practitioners. Though he himself sympathised with the suggestion of extra payment for doctors over fifty he felt bound to point out that it would do away with the whole idea of merit, and he did not see how the £1½ million could be diverted to a completely different purpose.

Obituary

JULES FREUND

M.D. Budapest.

Jules Freund died on April 22 in a hospital of the National Institutes of Health, Bethesda, Maryland, and with him died a pioneer in the field of immunology, whose name has become common coin among immunologists, by virtue of the technique he devised for enhancing antibody response.

He was born in 1890 in Budapest, where he qualified in medicine in 1913. After serving in the Austrian Army during the first World War he returned to Budapest as assistant professor of preventive medicine in 1917. In 1926 he went to the Henry Phipps Institute, Pennsylvania, and thereafter remained in the United States. In 1932 Freund became assistant professor of pathology at Cornell, and in 1938 assistant director of the Bureau of Laboratories in New York.

During these years, in addition to more or less routine work on public-health laboratory methods, and serum and vaccine production, he studied the basic mechanisms of allergic reactions, especially in relation to antibody fixation in the body. As a means of improving immunisation techniques he devised his well-known adjuvant method, by use of which he was able to produce the first fully authenticated experimental auto-immune disease—namely, testicular atrophy and sterility in guineapigs injected with their own testis material. He also studied experimental allergic encephalomyelitis, which was found to occur when poliomyelitis vaccines containing brain tissue were used in conjunction with his adjuvant.

When the Microbiological Institute of the National Institutes of Health changed its name and character, becoming the Institute of Allergy and Infectious Diseases, nobody was better suited than Freund to become chief of the laboratory of immunology. Soon after taking up the appointment in 1957 he became aware that he had multiple myeloma, but he continued to work in the laboratory and with his colleagues, and to stimulate

research throughout the National Institutes of Health until his death. In October, 1959, he was honoured by receipt of an Albert Lasker Award of the American Public Health Association.

Jules Freund was approachable, kindly, and always interested, with an infectious enthusiasm. He and his wife Betsy, who was his great support, were much loved by many friends. His widow and his son, Dr. Thomas Freund, survive him.

J. H. H.

WILLIAM GRANT WAUGH

M.A., M.D. Edin., F.R.C.S.E.

Mr. W. Grant Waugh, who practised both in Durham and in London, died on April 25 in Alberta, Canada. He was 73 years of age.

T. G. L. writes: "Bill Waugh was a general practitioner, a G.P. surgeon, and a surgeon. Courteous, gentle, friendly, and a natural aristocrat, he seemed a survival of some *ancient régime*, until a gleam of wit or a quiet remark revealed once more how up-to-date he had kept his mind. His interests were not limited to the town where he practised, nor his intellect to his profession. He held positions in a number of hospitals in Co. Durham, and had a practice in Harley Street. He was equally at home with his patients at both extremes. He tackled a fracture, a uterine prolapse, a kidney stone, an empyema, or a peptic ulcer with equal enthusiasm. He described an original plastic repair of a popliteal aneurysm, and a new biochemical approach to the osteoarthritic joint. He was a good judge of horseflesh (without being 'horsey'), and at one time would remark with pleasure that he owned half of one. He did, in fact, combine his interests on one occasion. His researches into the injection treatment of arthritis were first put to the test on a retired hunter, almost immobilised by arthritis. After injecting the knees, he mounted at once and took her 'over the sticks', thus staking his theories, his patient, and his own neck on the result. He was widely read, both inside and outside medicine. He contributed with perception, humanity, and facility to the clinical sections and correspondence columns of medical journals. His last 'blast on the trumpet'—challenging, but melodious as ever—showed that there was no decline in his powers. Was it fully appreciated, perhaps, that he could 'get something to bite upon' and still keep his tongue in his cheek?

"It is less than two years since Sunderland lost him, for he joined his son, Dr. Ian Grant Waugh, to start a fresh life in Canada at seventy. Our last news was of a new appointment in surgery at the local hospital. Now the profession has lost him, and is fast losing his type. He was one of the best of the Old Brigade, and we who follow will do well, if we do as well as he did."

Appointments

ADAMS, AILEEN K., M.B. Sheff., F.F.A. R.C.S., D.A.: part-time consultant in anæsthetics, Addenbrooke's Hospital, Cambridge.
BARROW, JACK, M.B. Lond.: assistant, department of venereal diseases, St. Thomas' Hospital, London.
EVANS, A. J. M.B. Lond., D.A.: assistant, department of venereal diseases, St. Thomas' Hospital, London.
FORBES, R. Y., L.R.C.P.E., D.P.H.: depute M.O.H., Aberdeen.
JOHNSTON, E. N. M., M.B. Cantab., M.R.C.P.: part-time consultant dermatologist, Nottingham and Mansfield hospital areas.
LEIPER, JOHN, M.B.E., M.B. Lpool, D.P.H.: county M.O., Cumberland.
NEWBERRY, R. G., M.B. Lond., D.P.H.: deputy M.O.H., school M.O., and deputy port M.O., Great Yarmouth.
TREHARNE, ANNE E., M.B. Manc., D.C.H.: school M.O., Manchester.
WILKINSON, R. H., M.D. Cantab.: consultant chemical pathologist, United Oxford Hospitals.

Birmingham Regional Hospital Board:

BOURKE, J. D., M.B. N.U.I., F.F.A. R.C.S.: part-time consultant anæsthetist, Birmingham (Dudley Road) group of hospitals.
DAVIS, F. J., M.R.C.S., F.F.A. R.C.S.: part-time consultant anæsthetist, Shrewsbury group of hospitals and Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry.
LOWE, H. G., M.B. Manc., F.R.C.S.: part-time consultant orthopædic surgeon, Stafford group of hospitals.
NOBLE, M. J. D., M.B. Edin., F.R.C.S.E., M.R.C.O.G.: part-time consultant obstetrician and gynæcologist, Birmingham (Dudley Road) group of hospitals.

Diary of the Week

MAY 8 TO 14

Sunday, 8th

INSTITUTE OF LARYNGOLOGY AND OTOLOGY, 330, Gray's Inn Road, W.C.1
10.15 A.M. Mr. Maxwell Ellis: Common Ear, Nose, and Throat Conditions.

Monday, 9th

POSTGRADUATE MEDICAL SCHOOL OF LONDON, Ducane Road, W.12
4 P.M. Prof. Feodor Lynen: Co-enzyme A and Fat Metabolism.
WRIGHT-FLEMING INSTITUTE OF MICROBIOLOGY, St. Mary's Hospital Medical School, W.2
5 P.M. Prof. Albert Neuberger: Digestion and Absorption of Protein in Normal Man and in Some Pathogenic Conditions. (Almroth Wright lecture.)

Tuesday, 10th

ROYAL COLLEGE OF SURGEONS OF ENGLAND, Lincoln's Inn Fields, W.C.2
5.45 P.M. Prof. G. J. Cunningham, Prof. P. C. Koller, Dr. R. J. C. Harris: Cell, Chromosome, and Virus Microscopy in Cancer Research.
ROYAL SOCIETY OF MEDICINE, 1, Wimpole Street, W.1
5.30 P.M. *Experimental Medicine & Therapeutics.* Dr. M. Vogt, Dr. P. B. Bradley, Dr. D. M. Leiberman: Reserpine.
8 P.M. *Psychiatry.* Dr. T. M. Ling, Dr. John Buckman: Individual Psychotherapy with LSD. Dr. Joshua Bierer, Dr. I. Browne: Treatment of Psychotic, Psychopathic and Emotionally Immature Patients with LSD and Group Psychotherapy in a Night Hospital Setting.
ST. MARY'S HOSPITAL MEDICAL SCHOOL
5 P.M. Dr. H. A. Davidson: Male Infertility and Postcoital Examination.
INSTITUTE OF DERMATOLOGY, Lisle Street, W.C.2
5.30 P.M. Dr. P. E. Bodkin: Applied Physics.
BIRMINGHAM MEDICAL INSTITUTE, 36, Harborne Road, Edgbaston, Birmingham.
8 P.M. *Psychiatry.* Dr. Leopold Stein: Evolution of Human Language.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Queen's College, Dundee.) Dr. Thue Poulson (Copenhagen): Aspects of the Treatment of Mitral Stenosis.

Wednesday, 11th

UNIVERSITY OF LONDON
5 P.M. (St. Mary's Hospital Medical School) Prof. G. W. Thorn: Current Concepts—Glucocorticoids and Gluconeogenesis.
5.30 P.M. (School of Pharmacy, 29, Brunswick Square, W.C.1.) Prof. H. B. Van Dyke (New York): Neurohypophyseal Hormones of Vertebrates.
ROYAL SOCIETY OF MEDICINE
2.30 P.M. *Proctology.* Dr. E. R. Cullinan, Mr. Tom Rowntree, Prof. John Bruce, Mr. R. W. Raven: Medical Management and Indications for Surgery in Diverticulosis and Diverticulitis.
POSTGRADUATE MEDICAL SCHOOL OF LONDON
2 P.M. Dr. K. Weinbren: Regeneration of the Liver.
ROYAL FREE HOSPITAL, Gray's Inn Road, W.C.1
5 P.M. Dr. J. L. Fahey (Bethesda): The Nature of Antibodies in Man.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. Henry Haber: Eosinophilic Granulomas of the Skin.
INSTITUTE OF DISEASES OF THE CHEST, Brompton, S.W.3
5 P.M. Dr. J. C. Batten: Amyloid and the Lung.
UNIVERSITY OF OXFORD
5 P.M. (Radcliffe Infirmary.) Prof. R. A. McCance: Development of Acid Base Control. (Litchfield lecture.)
UNIVERSITY OF LEEDS
3 P.M. (General Infirmary at Leeds.) Sir Howard Florey: Contributions of the Electron Microscope to the Understanding of Pathological Processes.

Thursday, 12th

ROYAL COLLEGE OF SURGEONS OF ENGLAND
5 P.M. Mr. N. C. Tanner: Technique and Late Results of Porto-Azygos Disconnection of Œsophageal Varices. (Hunterian lecture.)
ROYAL SOCIETY OF MEDICINE
5 P.M. *Ophthalmology.* Mr. F. D. McAuley, Mr. Kenneth Newton, Mr. John Watson: Treatment of Tumours of the Eyelids.
POSTGRADUATE MEDICAL SCHOOL OF LONDON
4 P.M. Dr. F. Avery Jones: Hæmatemesis and Melæna.
INSTITUTE OF DERMATOLOGY
5.30 P.M. Dr. William Frain-Bell: Benign Skin Conditions Requiring Radiotherapy.
UNIVERSITY OF ST. ANDREWS
5 P.M. (Queen's College, Dundee.) Dr. J. H. Hutchison: Cretinism and Juvenile Myxœdema.

Friday, 13th

POSTGRADUATE MEDICAL SCHOOL OF LONDON
10 A.M. Mr. Lawrence Abel: Cancer of the Rectum.
INSTITUTE OF LARYNGOLOGY AND OTOLOGY
3.30 P.M. Mr. J. C. Hogg: Sinusitis.
5.30 P.M. Dr. G. H. Howells: Significance of Orbital Swellings in Nasal Accessory Sinus Disease.

Saturday, 14th

FELLOWSHIP OF POSTGRADUATE MEDICINE
10 A.M. (St. Stephen's Hospital, Fulham Road, S.W.10.) Prof. C. E. Dent: Metabolic Bone Disease Presenting as Vaguely Localised Pain. (Inaugural lecture of a weekend course in rheumatic diseases.)

Births, Marriages, and Deaths

DEATH

HOGG.—On April 27, William James Hogg, M.D., of Forest Hill, Stonehaven, regional medical officer, Department of Health for Scotland.

Notes and News

FOR THE YOUNG

LAST Friday the King George's Jubilee Trust launched a silver jubilee appeal—the first national appeal since its foundation. As the Duke of Gloucester, the chairman of its council, has explained, this jubilee "will provide the occasion, and the means for reminding the adult community of their personal and individual responsibility for young people, and the young people themselves of their responsibility, as good citizens, to the community". The object of the Trust is "the advancement of the physical, mental, and spiritual welfare of the younger generation in the United Kingdom". It has spent more than £1 million in grants, but "the greatly increased number of young people and the practical effect of the decline in the value of money" have made its income of about £40,000 "wholly inadequate to meet the growing needs". A further £110,000 is wanted—particularly from contributions under covenant, from regular subscriptions, and from increased capital. Particulars may be had from the appeal secretary at St. James's Palace, London, S.W.1.

The main object of the Trust is to help boys and girls who leave school at 15. Many of these lack opportunities to develop their good qualities, and these opportunities "must be brought within the reach of all, particularly those who are passing through the difficult time of transition from school to work".

"Now, when increasing numbers of our boys and girls are entering employment, when public attention is focused on the shortcomings of at least some of them and when National Service is drawing to an end, is the opportune time to try imaginatively to arouse the interest of all young people in the qualities which make for good citizenship".

NUFFIELD TRAVELLING FELLOWSHIPS FOR GENERAL PRACTITIONERS

As part of its programme for the advancement of health, the Nuffield Foundation has generously given about £50,000; and, together with the College of General Practitioners, a scheme has been devised to enable general practitioners to undertake postgraduate study overseas during the next 4 years. Twelve awards are for men or women from Great Britain, and one similar award will be made in rotation each year for a doctor from Australia, New Zealand, Canada, or South Africa. The expenses of travelling and living will be met for the doctors (and their wives), and provision will be made for a locum for the general practitioners from this country.

The first awards to men and women of the United Kingdom will be:

Three *fellowships* (each for a period of 6 consecutive months) to enable general practitioners of outstanding ability, preferably between the ages of 35 and 45, to study overseas from July to December, 1961, in some subject of importance to general practice. The fellowship will cover for the fellow (and for his wife) tourist return travel by air, and other fares at tourist rates, together with an adequate subsistence allowance.

Three *assistantships* to enable doctors to gain experience as locum tenens in the practices of the fellowship holders. The value of the assistantship award will be up to £750 for 6 months, in addition to travelling expenses.

Applications for these awards must reach the Foundation by Oct. 31, 1960. The conditions of the fellowships and assistantships, and application forms, may be had from Mr. L. Farrer-Brown, The Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1.

PROGNOSIS FOR ALCOHOLICS

WHAT can a systematic course of 'Antabus' (disulfiram) treatment achieve, and can the prognosis in a given case of alcoholism be stated numerically? Berglin[1] goes some way towards answering both these questions. From some 650 alcoholics given disulfiram treatment under the auspices of the Gothenburg municipal authorities and other bodies he selected 126 for an intensive statistical study made by a social worker who visited the patient's home with a questionary of 60 items. A year after the completion of treatment, 31% of the 126 had achieved complete abstinence, and another 31% some improvement. The remaining 38% were no better and most of them later required institutional treatment. The answers to the 60 questions, by the alcoholic himself, or his immediate contacts, yielded information about his past and present and thus gave clues to his future. These clues are presented as so many points, good or bad, from which a numerical prognosis can be built up. Minus points were earned by a history of drink before the age of 21 (25 points down). Other items on the minus side were a record of more than five bouts of drinking, the employment of some alternative beverage such as methylated spirits (19 points down), previous residence in some institution, a state of tension when sober, and a carefree attitude of psychoinfantile indifference to the problem of alcohol. The importance attached to this last point was so great that it was down 40. Factors earning the alcoholic plus points make more cheerful reading. If he had a record of sobriety during the first forty years of his life he could be marked 11 points up. As many as 27 plus points could be allotted to the patient whose output of work during treatment was satisfactory. Matrimony improved the prognosis by 13 points. Berglin ends on a hopeful note by pointing out that all is not necessarily lost even when minus points tot up to a formidable total.

1. Berglin, C. G. *Svenska Läkartidn.* March 11, 1960

University of Glasgow

On April 30 the degree of M.D. was conferred on I. A. Porter.

Royal College of Physicians of London

At a comitia of the college on April 28, with Sir Robert Platt, the president, in the chair the following were elected to the fellowship:

W. S. WHIMSTER, Nottingham; J. C. J. MCENTEE, London; L. G. NORMAN, London; W. A. HAWK, Canada; P. W. HUTTON, Uganda; RUSTOM JAL VAKIL, India; BRIAN MCARDLE, London; Lord TAYLOR of HARLOW, London; N. F. COGHILL, London; Brigadier MOHAMMAD SARWAR, Pakistan; ROBERT MOWBRAY, Durham; E. B. FRENCH, Edinburgh; Sir STANFORD CADE, London; A. A. G. LEWIS, London; THOMAS PARKINSON, Harpenden; ARTHUR JORDAN, Sheffield; L. L. REES, London; R. B. THOMPSON, Newcastle upon Tyne; M. E. MACGREGOR, Warwick; D. A. R. POND, London; W. E. HENLEY, New Zealand; B. D. R. WILSON, London; Major-General A. N. T. MENECES, R.A.M.C., Chester; C. W. M. WHITTY, Oxford; R. R. H. LOVELL, Australia; LENNOX EALES, South Africa; C. H. EDWARDS, London; J. M. JEFFERSON, Birmingham; P. F. BORRIE, London; J. L. FREW, Australia; J. P. SHILLINGFORD, London; H. L. ELLIS, Oxford; J. D. S. CAMERON, Edinburgh; A. E. MOURANT, London; HAROLD SCARBOROUGH, Cardiff; D. F. CAPPELL, Glasgow; R. G. MACFARLANE, Oxford; Sir CLEMENT PRICE THOMAS, London; ARVID WALLGREN, Stockholm.

The following having satisfied the censors' board were elected to the membership:

June P. Arnold, M.D. Lpool, Bryan Ashworth, M.B. St. And., B. W. D. Badley, M.B. Lond., Michael Barry, M.B. Cantab., Michael Brown, M.B. Lond., A. A. Buchanan, M.B. Lond., Devendra Nathan Chanmugam, M.B. Ceylon, M.B. Lond., R. D. Cohen, M.B. Cantab., J. S. Comaish, M.B. Lpool, Joseph Connolly, M.B. Lond., G. H. Cooray, M.D. Lond., A. H. Dimond, M.B. Cantab., C. G. B. Downie, M.B. Edin., Amal Kumar Dutta, M.B. Calcutta, A. T. T. Forrester, M.B. Lond., Lionel Fry, M.B. Lond., Malay Bhushan Ghosh, M.B. Calcutta, Binod Kumar Gupta, M.B. Lucknow, H. M. Hodkinson, B.M. Oxon., E. E. Jones, M.B. Lond., Abdel Salam Rafiq Kamhawi, M.D. Beirut, H. J. Liebeschuetz, B.M. Oxon., D. R. London, B.M. Oxon., J. N. MacCaig, M.B. Manc., A. G. Malleson, M.B. Lond., Valerie J. Marrian, M.B. Edin., P. D. Marsden, M.B. Lond., N. M. C. Mayne, M.B. Birm., G. A. H. Miller, B.M. Oxon., M. G. Miller, M.B. Lond., R. O. Moore, M.B. N.Z., P. M. J. O'Brien, M.B. Lond., A. T. Otaki, M.B. Lond., M. S. N. Pathy, M.R.C.P.E., O. H. D. Portsmouth, M.B. Lond., A. I. Rae, M.B. Lond., Gordon Ross, M.B. Lond., Leo Stimmler, M.B. Lond., Fred Stratton, M.D. Manc., Mailoo Visuvaratnam, M.B. Ceylon, J. G. Walker, M.B. Lond., J. M. Walker, M.B. Birm., R. E. O. Williams, M.D. Lond., Poi Kwong Wong, M.B. Malaya, E. G. Wooster, M.B. Cantab.

Licences to practise were conferred on the 178 candidates who have passed the final examination of the Conjoint Board:

M. F. A'Brook, A. P. Adams, E. J. J. Almeida, J. J. R. Almeyda, Elisabeth M. Appleby, Jean Arnold, Keith Arthur, N. H. Atkinson, Raphael Balcon, M. A. Barnett, John Barrett, J. M. Barry, Ann A. Barton, Aref Sa'd Bataineh, Brian Batten, Pauline J. Begley, H. E. Berry, Delia A. M. Bickerton, John Bienenstock, Jean M. Bird, R. C. Bland, Gerald Blandford, Barbara M. Bonner-Morgan, P. N. Booth, W. J. Boyle, F. E. Bruckner, Jill A. Bullimore, M. J. Campbell, P. C. Cann, D. McD. Cardwell, A. A. Carrasco, J. A. Carter, P. G. Cassell, D. N. Challacombe, H. M. Clink, C. L. Colton, A. R. Cook, D. E. Cooksley, Dorothy J. Cooper, T. B. Cork, Sheila A. Corrin, Helena M. J. Cotter, J. E. Crockett, J. C. Cummins, M. F. Cuthbert, D. J. W. Darby, R. N. Davies, Jill Dean, P. B. Deverall, Sybil B. Diggle, Ewa M. Dragowska, B. R. Duncan, E. C. Emelife, A. W. G. English, J. D. Eustace, C. E. Evans, P. O. Fasan, R. E. Faulkner, I. T. Field, H. M. Fisher, T. R. Fisher, D. M. Flanagan, Sally E. Flew, K. G. E. Frohnsdorf, Janet K. Gambell, D. H. Georgelin, B. E. Gilliver, Sharron H. Gilmour, J. C. Gingell, P. L. Girolami, Akude Gletsu, R. A. Goldfinch, R. J. Green, Susan R. Greenwood, R. N. Grunerberg, A. D. G. Gunn, Pamela M. Haigh, T. R. Hailstone, J. E. Hale, J. M. Hawkins, Alethea B. Heal, Joseph Herbert, Rosemary E. Heron, R. D. Hill, B. L. Houghton, R. H. Hughes, G. A. Hunter, I. M. James, M. L. James, Cecily A. Jenkins, B. D. Jones,

H. H G. Jones, H. D. Kaufman, M. J. Kestle, Edvina M. King, Thilla Krikler, D. A. H. Langman, Alan Levine, D. J. Lightman, M. J. Lipton, J. S. P. Lumley, Lawrence Lupin, Leonie M. McEwen, M. T. MacMahon, I. F. Macrae, D. J. Martin, M. H. J. Martin, R. C. Martin, C. A. S. Mason, J. R. Massy, C. D. Matthews, Labhshanker Sukhlal Mehta, G. M. Michael, B. S. Michaels, J. S. Musgrove, Daphne M. Newman, May Ning, E. R. Norton, V. B. Odunlami, M. J. Oliver, J. D. Parry, Catherine S. Peckham, M. J. Pemberton, Jean P. Pettavel, Sally J. Phillips, Dianne E. Philp, Jeremy Pilcher, C. J. F. Pool, David Prothero, A. R. Reece, G. M. Rees, Gunnar Reiman, D. S. Restall, Christine E. Riley, I. E. W. Robertson, R. E. Robinson, N. C. Roles, Wendy Roles, J. B. Sales, Naguib Abdelmalek Samaan, Elizabeth Shindler, A. J. Simmonds, G. W. Simonds, D. H. Smith, Joanna South, P. E. Spicer, Charmian R. L. Stephens, Patricia S. Stephenson, Anne K. Stewart, K. E. Tanner, W. H. Thomas, Ada A. Thornton, C. J. Todes, D. A. Toms, L. N. Travis, K. L. K. Trick, Irene J. Tufft, William Ursell, J. A. S. Vick, H. Wagman, A. E. Walker, D. E. Walter, M. M. Watkins, W. N. D. Watson, J. L. Wearn, P. C. Weaver, C. L. W. Webb, Paul Wentworth, B. W. Whalley, N. R. Whiting, J. N. Whittaker, A. R. F. Williams, Wendy E. Williams, R. A. Wiseman, Bridget M. Wood, R. B. Woodd-Walker, M. W. G. Wren, C. H. Young.

The following diplomas and those mentioned in our issue of April 30 (p. 988) were conferred jointly with the Royal College of Surgeons:

D.L.O.—Maung Maung Myint.
D.O.—P. W. E. Downes.
D.T.M. & H.—Johannes Olafsson.

On Tuesday, June 21, at 5 P.M., at the college, Pall Mall East, S.W.1, Dr. J. G. Scadding will give the Mitchell lecture. He will speak on *Mycobacterium tuberculosis* in the ætiology of sarcoidosis.

Royal College of Surgeons in Ireland

Faculty of Anæsthetists.—This faculty has been instituted by the college and the following have been elected to the board:

Dean, Dr. T. J. Gilmartin; vice dean, Dr. V. O. McCormick; Dr. P. Drury Byrne, Dr. P. Nagle, Dr. S. Kenny, Dr. P. Murray, Dr. J. A. Woodcock, Dr. R. Davys, Dr. J. W. Dundee, Dr. S. H. Love; council representative, Mr. D. J. Riordan; ex-officio, Mr. T. G. Wilson, Mr. S. F. Heatley.

The president and council of the college will give Carmichael prizes of £150 and £100 for the best essays on the state of the medical profession in its different departments of physic, surgery, and pharmacy in Great Britain and Ireland, the state of the hospitals and schools of medicine, surgery, and pharmacy, and the state and mode of examination or of testing the qualifications of candidates of the different licensing colleges or corporations of medicine, surgery, and pharmacy. Further particulars may be had from the registrar of the college, Dublin.

British Association of Physical Medicine

Proposing the health of The Association at its annual dinner held at Apothecaries' Hall on April 29, Mr. Derek Walker-Smith, the Minister of Health, spoke of the steadily growing interest in disorders of the locomotor system, dating from the first world war. The medical progress made has been greatly helped by the Association with its specialised forum. Now that people live longer they must not be passive survivors but must pursue positive health and active wellbeing.

Dr. Hugh Burt, the president, said that physicians practising physical medicine are having more and more cases referred to them for diagnosis, not merely for treatment; and those entering the specialty need a sound knowledge of medicine as a whole. When the National Health Service started, there were 45 consultants in the subject but now there are 100, and a committee at present sitting may well propose that there should be more. For a time orthopædic surgeons regarded practitioners of physical medicine with some suspicion, just as they themselves were once regarded with suspicion by general surgeons. But bridging of the gulf " is of vital importance to the patients whom we both see "; and as evidence of it he welcomed the presence at this dinner, for the first time, of the president of the British Orthopædic Association, Mr. H. J. Seddon.

Squadron-leader C. B. Wynn Parry, in his amusing account of The Guests, also welcomed Mr. Seddon, whom he described as " late instructor in surgery in the University of Michigan ". Dr. F. Dudley Hart, responding, showed the wide range of interests suitable to a president of the Heberden Society. The later phases of the evening had, he noted, induced a look of distaste on the face of James I, whose portrait hangs behind the high table, and whose *Counterblast to Tobacco* appeared 350 years before Doll and Bradford Hill.

Royal Society of Medicine

Richard Kovacs prize (£50).—This prize is awarded triennially for work in physical medicine. Applications should reach the hon. secretary of the section of physical medicine, 1, Wimpole Street, London, W.1, by Sept. 30.

Royal Society

Prof. Ragnar Granit, of Stockholm, has been elected a foreign member of this society for his researches on the physiology of vision and neurophysiology.

Glasgow Medical Exhibition

The organisers of the London Medical Exhibition are to hold their annual regional medical show this year in Glasgow. Mr. Arthur Jacobs, P.R.F.P.S., will open it in the St. Andrew's Hall, on Monday, May 23, at 2.45 P.M. It will remain open till May 27.

First International Congress of Histochemistry and Cytochemistry

This congress will be held from Aug. 28 to Sept. 3 in Paris. Further particulars may be had from the secretary-general, Dr. R. Wegmann, Institut d'Histochimie Médicale, 45, rue des Saints-Pères, Paris (6e), France.

A weekend study course for those engaged in mental hospital therapeutic community work will be held at Burton Manor Residential College for Adult Education, Wirral, Cheshire, from July 1 to 3. The theme of the course will be Whither Psychiatry? The speakers will include Dr. Russell Barton, Dr. C. R. Lowe, Prof. Thomas McKeown, Dr. Richard Fox, Dr. Pamela Mason, Dr. Isaac Frost, and Dr. James Brown. Further particulars may be had from Dr. Frost, Deva Hospital, Liverpool Road, Chester, or Dr. George Egan, Liverpool Psychiatric Day Hospital, 10, Croxteth Road, Liverpool, 8.

Mr. R. Y. Calne, Dr. Reginald Hall, and Dr. I. C. Roddie have been awarded Harkness fellowships of the Commonwealth Fund tenable in the United States.

Prof. Ian Aird has left for Athens to help in the study of the projected school of postgraduate medicine at the Evangelismos Hospital. Later he is to visit Beirut as guest of the Middle East Conference of Surgeons.

The annual dinner of the Regional Hospitals' Consultants and Specialists Association was held at the House of Commons on April 29. Mr. Harold Dodd was in the chair, and the speakers included Lord Moran, Sir John Charles, Sir Stephen King-Hall, and Mr. Robert Cooke, M.P.

The International Endoscopy and Cineradiology Society will hold its annual congress on Wednesday, May 25, at 2.15 P.M., at 1, Wimpole Street, London, W.1, under the presidency of Dr. Frank Greenwood. The speakers will include Mr. H. G. Hanley. Further particulars may be had from the hon. secretary of the congress, Dr. Brian Stanford, 54, Upper Montagu Street, W.1.

The Older Worker and His Job.—This short popular account of recent research on the skills and abilities of the elderly worker, and in particular of the studies described by Mr. A. T. Welford in *Ageing and Human Skill* (see *Lancet*, 1958, ii, 1214), has been compiled by Hilary M. Clay for the Department of Scientific and Industrial Research (Problems of Progress in Industry series no. 7. H.M. Stationery Office, 1*s.* 5*d.* by post).

The poliomyelitis unit at Rush Green Hospital, Romford, Essex, have compiled a lively ward magazine, which has been typed by one of their members " by foot ". Its title, *Puffin*, is typical of the courage and cheerfulness of this small company of frog-breathers and iron-lung breathers. They are appealing for £1000 to buy a motorvan to take some of them " out and about ".

Copies of a new British standard for pressure steam sterilisers of small size (with independent steam supply) for unwrapped instruments and utensils (B.S. 3233: 1960) may be had (4*s.* each) from the British Standards Institution, Sales Branch, 2, Park Street, London, W.1.

CORRIGENDA: *Electronic Monitoring Apparatus for Coil Kidney.*—In the article by Mr. R. Brennand and Dr. N. V. Bunker (March 12, p. 578) footnote 3 should have read: Denison, A. B., Spencer, M. P. *Rev. sci. Instrum.* 1956, **27**, 707.

Infantile Structural Scoliosis.—The last paragraph of Prof. J. I. P. James' letter of April 16 should have begun: " Having seen well over 200 patients in ten years . . ."